Preimplantation Genetic Testing (PGT)

Avicenna Experience (2013-2020)

Saeed Reza Ghaffari

and

Maryam Rafati

Previous: Avicenna Biotechnology Research Institute, ACECR

Current: Clinical Genetics Branch, DCEG, NCI, NIH

Collaborators

Avicenna Infertility Center

- **Clinical Genetics Laboratories**
  - Saeed Reza Ghaffari, MD MSc PhD
  - Maryam Rafati, MD PhD
  - Faezeh Mohamadhashem PhD
  - Fatemeh Hoseininasab MD
  - Elaheh Rezvani MSc
  - Sanaz Abolfathi MSc
- **Infertility Treatment Clinic**
  - Soheyla Ansaripur, MD
- **Department of Embryology**
  - Mohammad Reza Sadeghi, PhD
  - Somayyeh Kazem Nejhad PhD

Hope Generation Foundation

- **Next-generation Sequencing Lab**
  - Saeed Reza Ghaffari, MD MSc PhD
  - Maryam Rafati, MD PhD
  - Azadeh Hoseini MSc

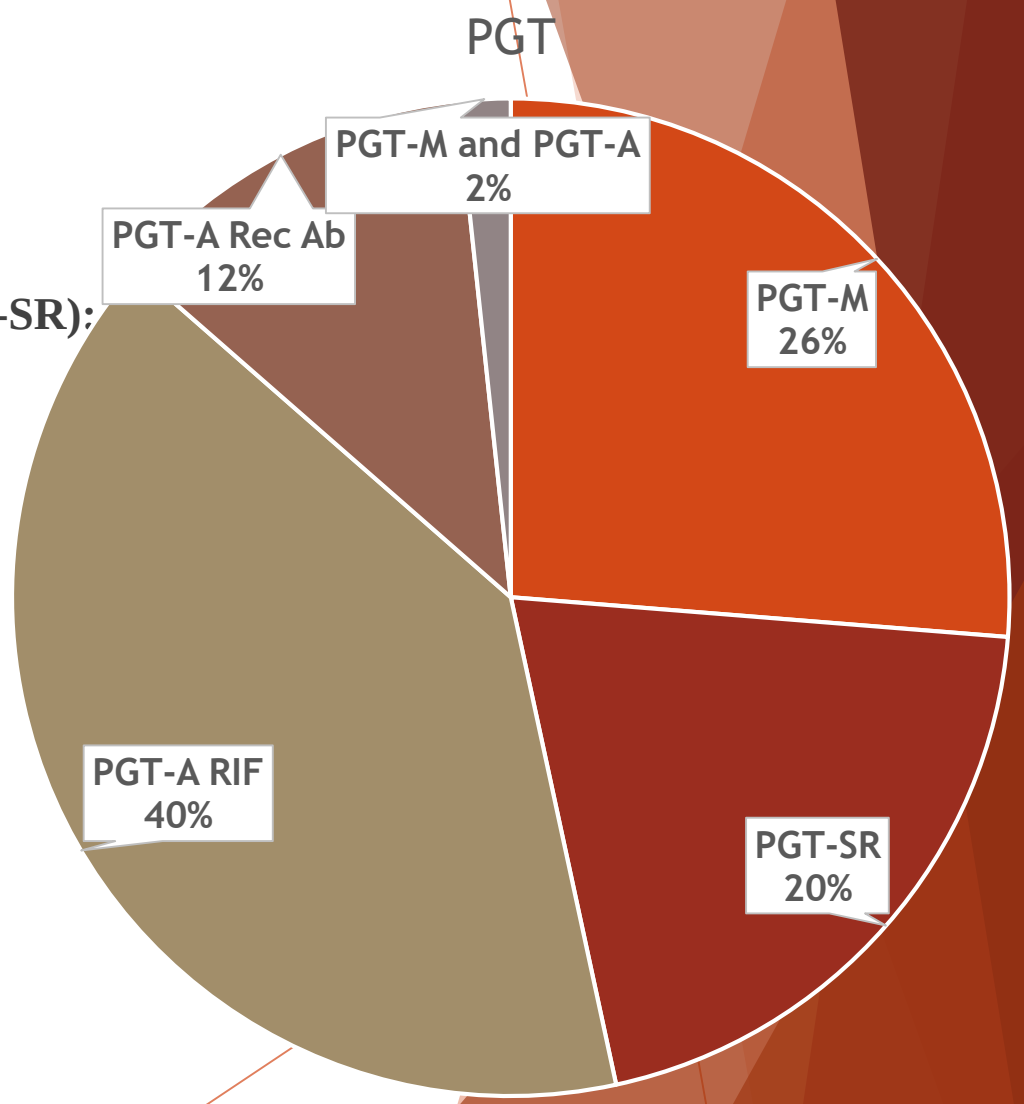
PGT

A group of genetic assays used to evaluate embryos before transfer to the uterus.

- **Preimplantation genetic testing-monogenic (PGT-M):**
  - Targeted to single gene disorders.
  - Uses only a few cells from the early embryo, usually at the blastocyst stage
  - Misdiagnosis is possible but rare with modern techniques.
  - **Confirmation of PGT-M results with chorionic villus sampling (CVS) or amniocentesis should** be offered.
- **Preimplantation genetic testing-structural rearrangements (PGT-SR):**
  - To detect structural chromosomal abnormalities such as translocations.
  - **Confirmation of PGT-SR results with CVS or amniocentesis should be offered.**
- **Preimplantation genetic testing-aneuploidy (PGT-A)**
  - To screen embryos for whole chromosome abnormalities.
  - **Traditional diagnostic testing or screening for aneuploidy should be offered** to all patients who have had PGT-A.

PGT , Avicenna experience

- **Preimplantation genetic testing-monogenic (PGT-M):**
  - **31 families**
- **Preimplantation genetic testing-structural rearrangements (PGT-SR):**
  - **24 couples with abnormal karyotype**
- **Preimplantation genetic testing-aneuploidy (PGT-A):**
  - Infertility or repeated implantation failure: **47**
  - Recurrent abortion: **14**
- **PGT-M and PGT-A: 2**
  - **PGD-PGS-NGS (Leber congenital amaurosis): 1**
  - **PGD-PGS-NGS (Meckel-Gruber syndrome): 1**

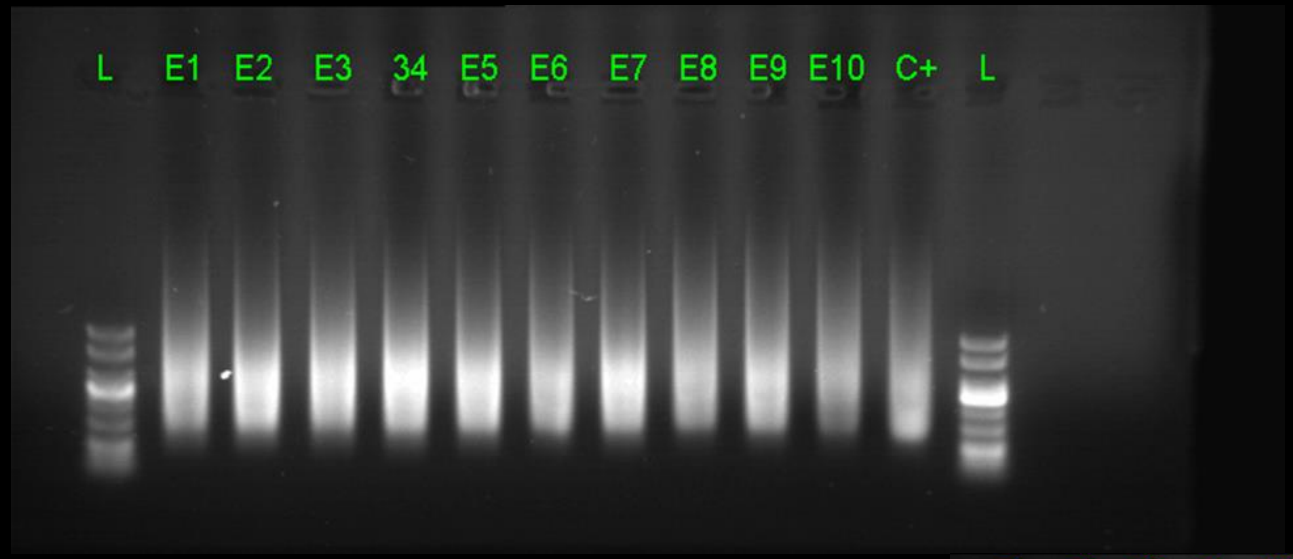


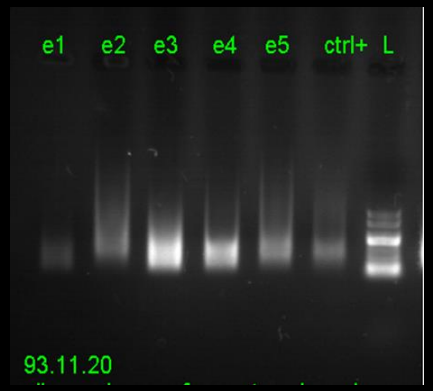
Avicenna Experience
Preimplantation genetic testing-monogenic (PGT-M)
(2013-2020)

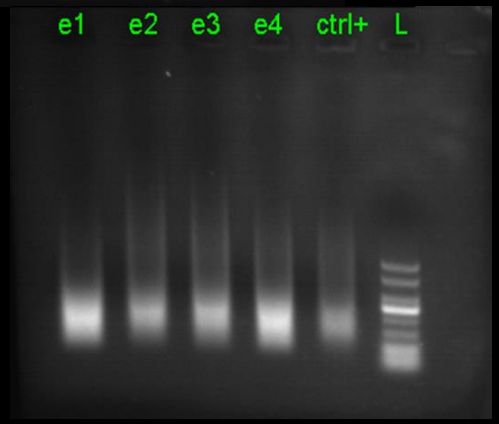
PGT-M

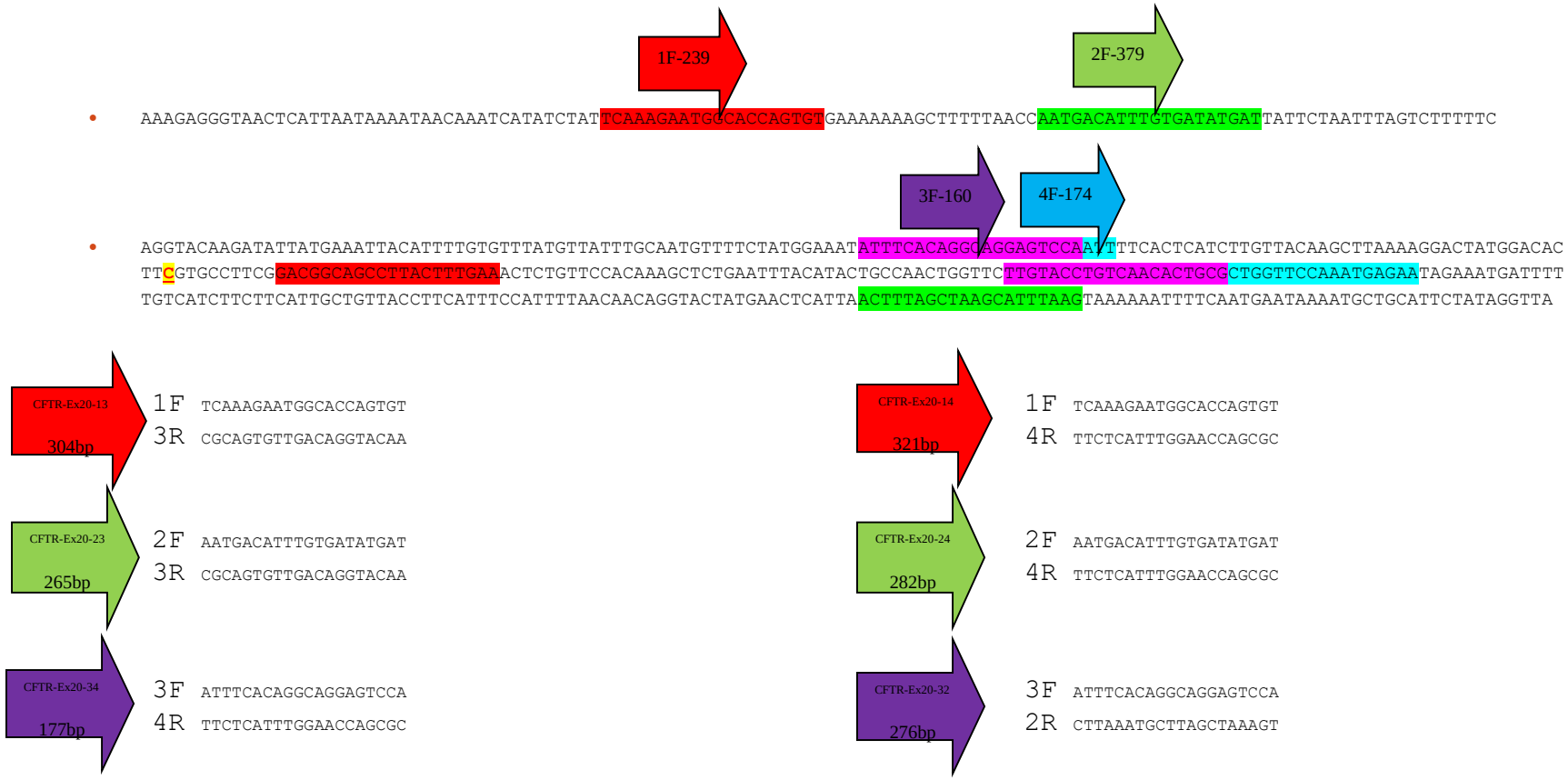
- PGT-M over time:
  - Old approach
    - Very small amount of DNA
    - One reaction per embryo
  - Comprehensive approach
    - **Single-cell whole genome amplification**
      - Large amount of high-quality DNA
      - Multiple testing on each embryo
      - Rule out of contamination

Whole Genome Amplification





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CFTR-Ex20-13
304bp
1F TCAAAGAATGGCACCAGTGT
3R CGCAGTGTTGACAGGTACAA
CFTR-Ex20-14
321bp
1F TCAAAGAATGGCACCAGTGT
4R TTCTCATTTGGAACCAGCGC
CFTR-Ex20-23
265bp
2F AATGACATTTGTGATATGAT
3R CGCAGTGTTGACAGGTACAA
CFTR-Ex20-24
282bp
2F AATGACATTTGTGATATGAT
4R TTCTCATTTGGAACCAGCGC
CFTR-Ex20-34
177bp
3F ATTTCACAGGCAGGAGTCCA
4R TTCTCATTTGGAACCAGCGC
CFTR-Ex20-32
276bp
3F ATTTCACAGGCAGGAGTCCA
2R CTTAAATGCTTAGCTAAAGT

Wide Range of Genetic Disorders

Examples of studied disorders:

- Beta-thalassemia
- Spinal Muscular Atrophy
- Duchenne Muscular Dystrophy
- Cystic Fibrosis
- Congenital Hearing Loss
- Achondroplasia
- **Metachromatic Leukodystrophy**
- **Meckle-Gruber Syndrome**
- **Leber Congenital Amaurosis**
- **Usher Syndrome type II**
- **Fibrodysplasia Ossificans Progressiva**

Even rare disorders

Workflow

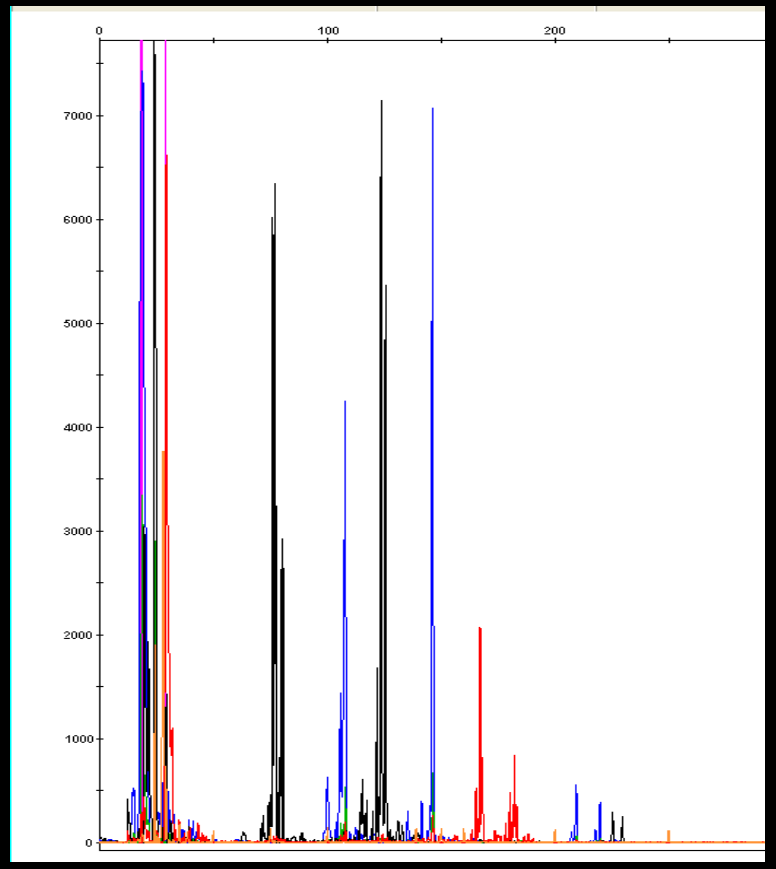
- Genetic Counseling

- Mutation detection or confirmation
- Design multiple primer sets
- STR profiling of the parents

- Whole genome amplification
- Subsequent investigations:
  - PCR amplification
  - Sequencing
  - STR profiling

Rule out of Contamination

STR Markers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100
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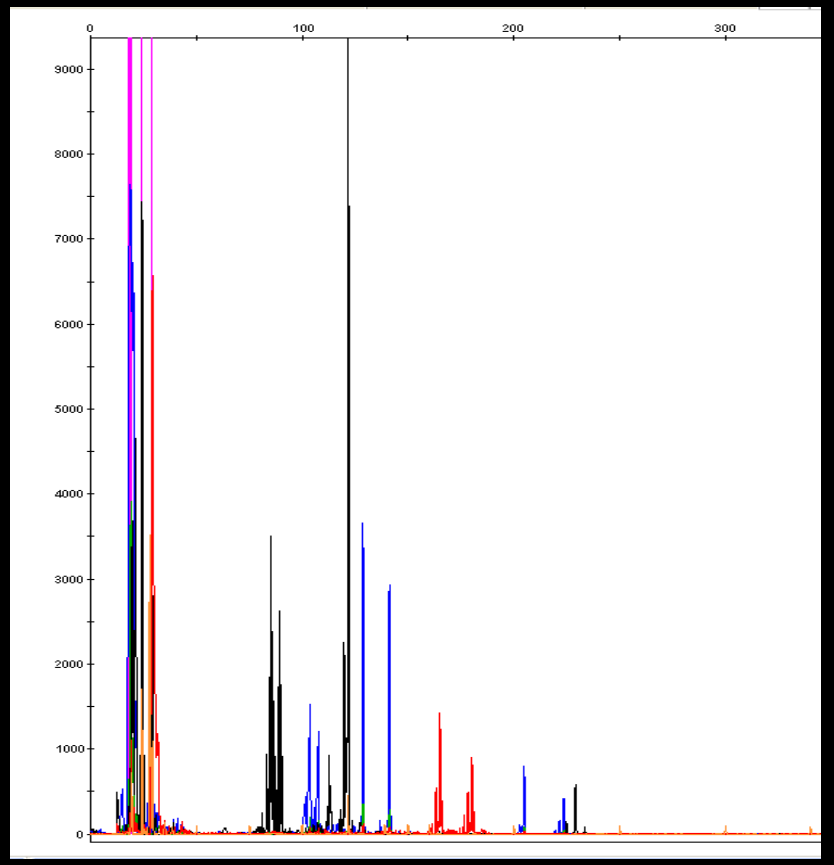
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7000
6000
5000
4000
3000
2000
1000
0

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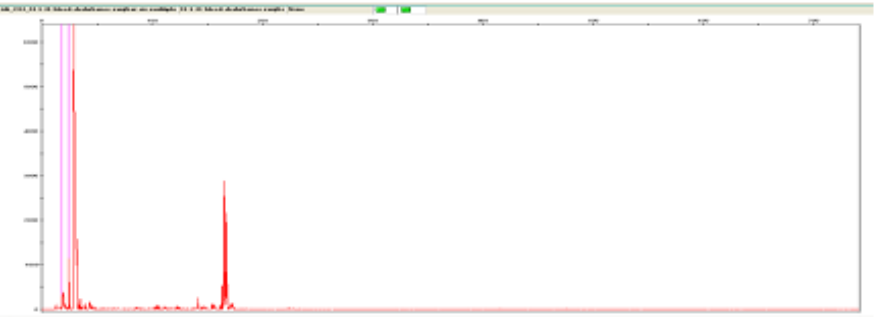
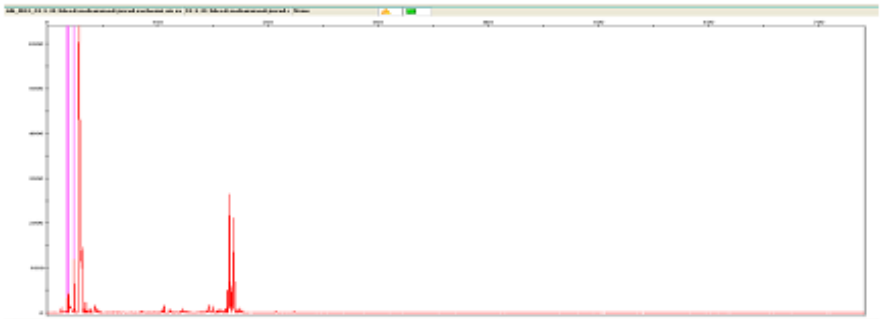
PGD (Beta Thalassemia)
…../…../2C-E1
STR Markers

Mother



2C-E1

Father



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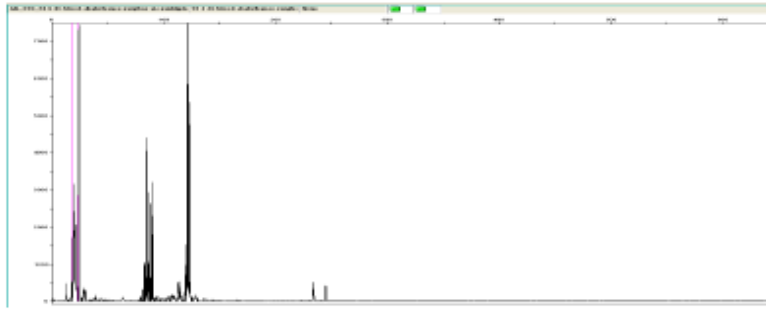

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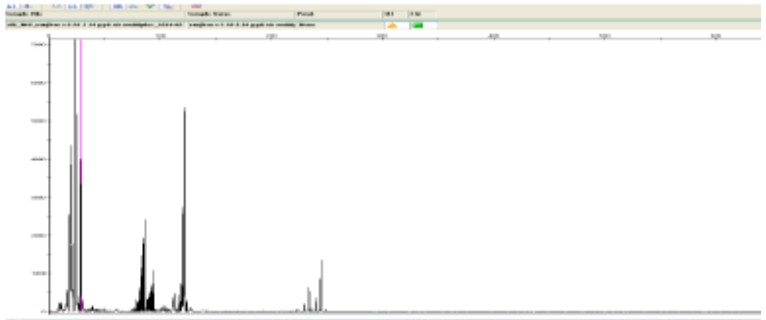

Father

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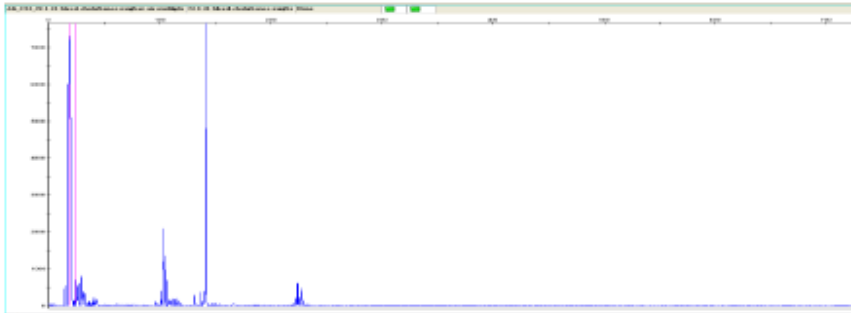
PGD (Beta Thalassemia)
…../…../2C-E1
STR Markers

Mother



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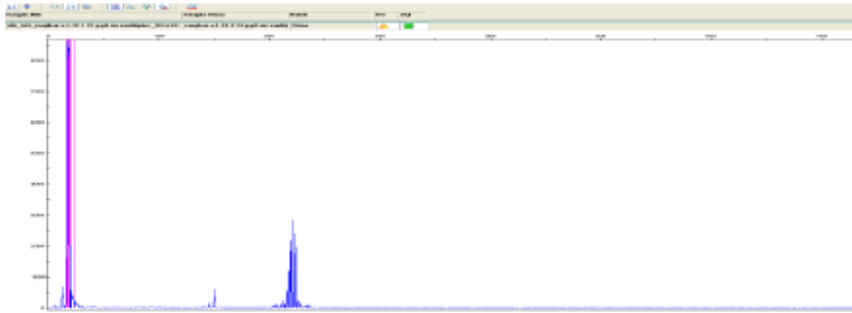

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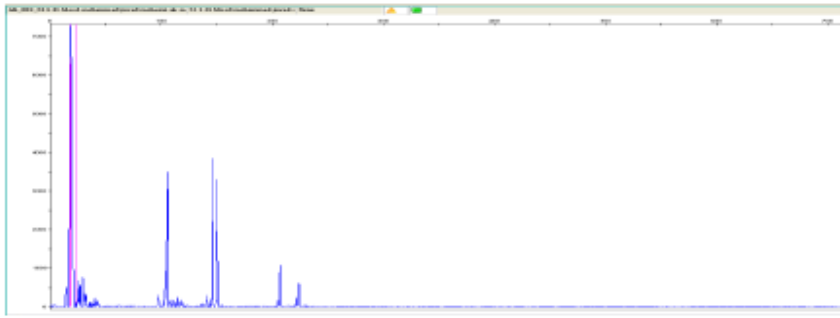

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PGT-M

Total families: **31**

- Beta Thalassemia: **21**
- SMA: **2**
- Meckel-Gruber Syndrome: **1**
- Leber Congenital Amaurosis: **1**
- Metachromatic leukodystrophy: **1**
- Usher Syndrome type II: **1**
- Hearing Loss: **2**
- Fibrodysplasia Ossificans Progressive: **1**
- Cystic Fibrosis: **1**

PGT-M

- No. of couples: **31**
- No. of studied embryos: **250**

- Successful single-cell Whole Genome Amplification: **229/250 (91.6%)**
- Embryos with conclusive results: **138/229 (60.2%)**
- No. of embryos without studied mutation: **72 (28.8%)**
- Average No. of transferable embryo/family: **2.3**

- Average maternal age: 29.5 Y
- No embryo transfer yet: 4 couples

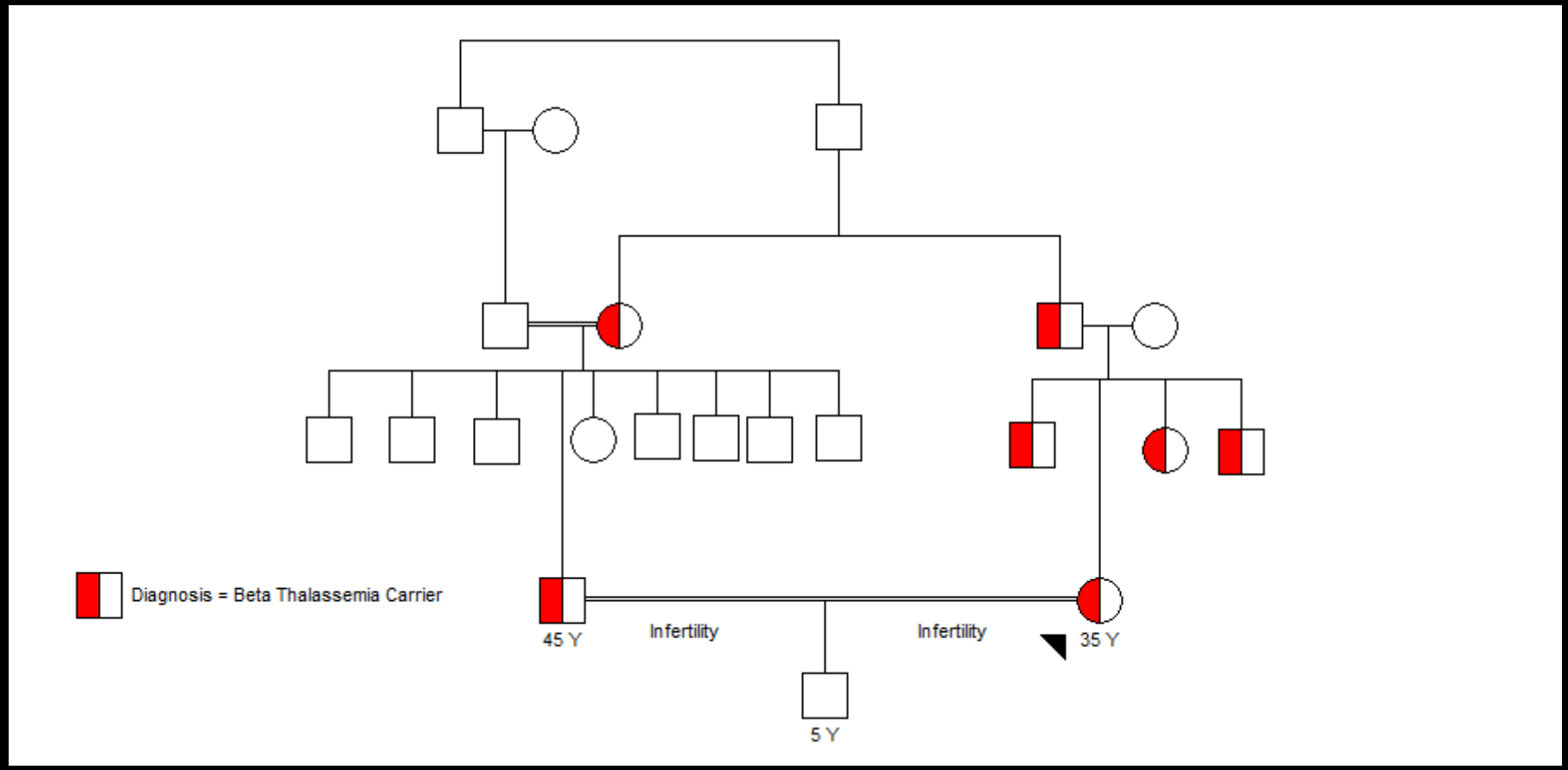
PGT-M

- ICSI cycles: 36
- Transfer cycles: **32**
  - 1 transfer cycle per family: 18
  - 2 transfer cycles per family: 4
  - 3 transfer cycles per family: 2

- Per ICSI cycle:
  - **Implantation rate : 6/27 (22.2%)**
  - **Clinical pregnancy/live birth rate: 6/27 (22.2%)**
  - Abortion Rate: 0/27 **(0%)**

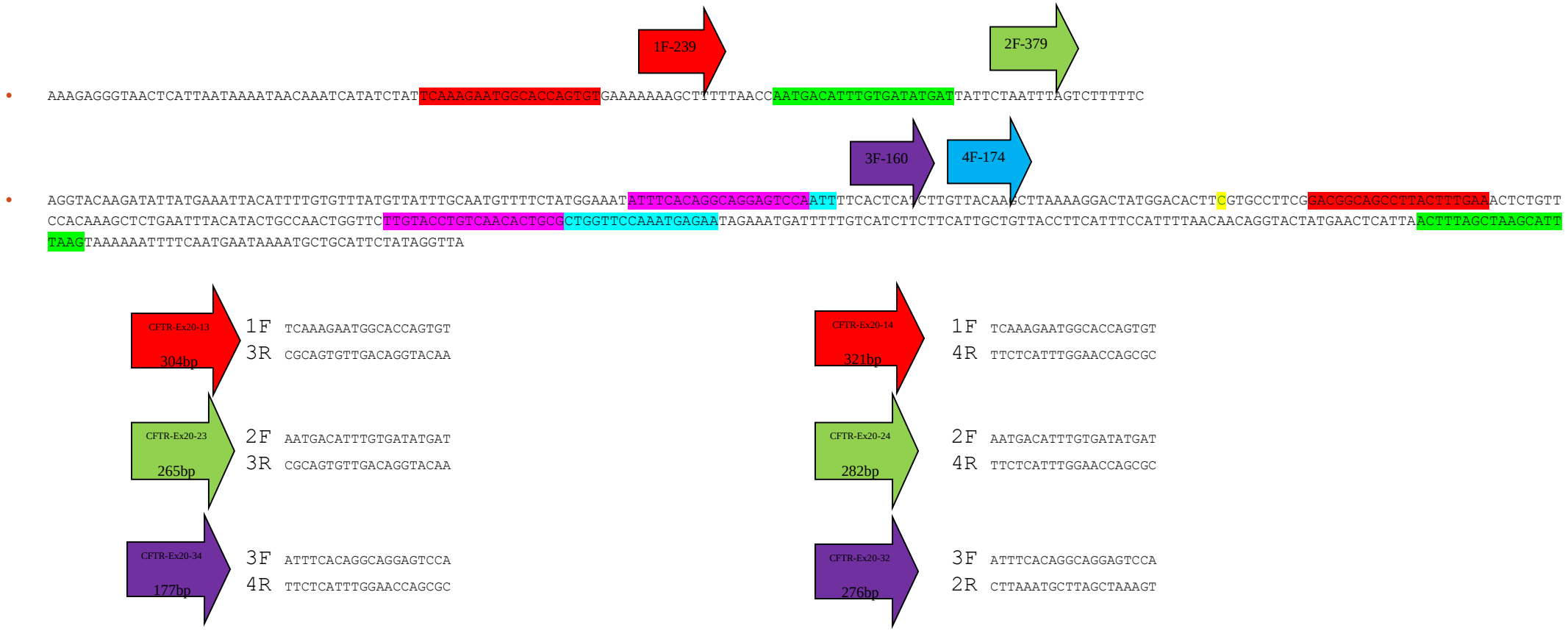
Examples

Pedigree


Diagnosis = Beta Thalassemia Carrier
45 Y
Infertility
Infertility
35 Y
5 Y

Mutation Detection

Patient ID	Mutation in HBB Gene	Genotype	Phenotype
Mother **(L-SH)**	c.112delT	Heterozygous	MCV: 63.9fl MCH: 18.8pg Hb A: 94.5% Hb A2: 5.0%
Father **(Gh-Ghe)**	c.112delT	Heterozygous	MCV: 58.3fl MCH: 15.9pg Hb A: 95.2% Hb A2: 4.0%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3F-160
4F-174
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CFTR-Ex20-13
304bp
1F TCAAAGAATGGCACCAGTGT
3R CGCAGTGTTGACAGGTACAA
CFTR-Ex20-14
321bp
1F TCAAAGAATGGCACCAGTGT
4R TTCTCATTTGGAACCAGCGC
CFTR-Ex20-23
265bp
2F AATGACATTTGTGATATGAT
3R CGCAGTGTTGACAGGTACAA
CFTR-Ex20-24
282bp
2F AATGACATTTGTGATATGAT
4R TTCTCATTTGGAACCAGCGC
CFTR-Ex20-34
177bp
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4R TTCTCATTTGGAACCAGCGC
CFTR-Ex20-32
276bp
3F ATTTCACAGGCAGGAGTCCA
2R CTTAAATGCTTAGCTAAAGT

Biopsy Checklist

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آزمایشگاه ژنتیک مولکولی

Family ID:

Whole Genome Amplification Method:

Laboratory Checklist

Father's name: [redacted]

Mother's name:

Family ID: 3308

Date: 95.12.19

❖ ***Embryo biopsy***

Date and time: 95.12.19

Done by:

checked by:

No	Subject	Embryo ID				
		E-1	E-2	E-3	E-4	E-5
1	Transfering the embryo to the labeled dish	9:39 Compact 2cells	9:36 12A 2cells	9:34 8B 2cells	9:30 12B 2 cells	9:27 10AB 2 cells
2	Transferring the blastomeres to the labeled microtube	9:58	10:—	10:2	10:3	10:4

No	Subject	Embryo ID				
		E-6	E-7	E-8	E-9	~~E-10~~
1	Transfering the embryo to the labeled dish	9:25 12A 2 cells	9:24 10B 2cells	9:21 Compact8 (1 cell)	9:24 compact (2 cells)	
2	Transferring the blastomeres to the labeled microtube	10:6	10:8	10:10		

Signed:

~~Embryologist~~

Dr Sadeghi

Geneticist

Dr Ghaffari

Checker

95.12.19

95.12.19

Freezing Checklist

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Family ID: [redacted]

Father's name: [redacted]

Mother's name:

Family ID: 33098

Date: 95.12.19

❖ *Embryo Frozen*

Date and time: 95.12.19

Done by:

checked by:

No	Subject	Embryo ID				
		E-1	E-2	E-3	E-4	E-5
1	Transfering the embryo to the labeled dish	11:43′	11:46′	11:50′	12:2′	12:5′
2	Transferring the embryo to the labeled cryotop	11:55′	11:58′	12	12:9′	12:11′

No	Subject	Embryo ID				
		E-6	E-7	E-8	E-9	E-10
1	Transfering the embryo to the labeled dish	12:7′	12:15′	12:17′	12:20′	
2	Transferring the embryo to the labeled cryotop	12:13′	12:23′	12:25′	12:28	

Signed:

Done by:

Checked by:

95.12.19

Single cell whole genome amplification (WGA)

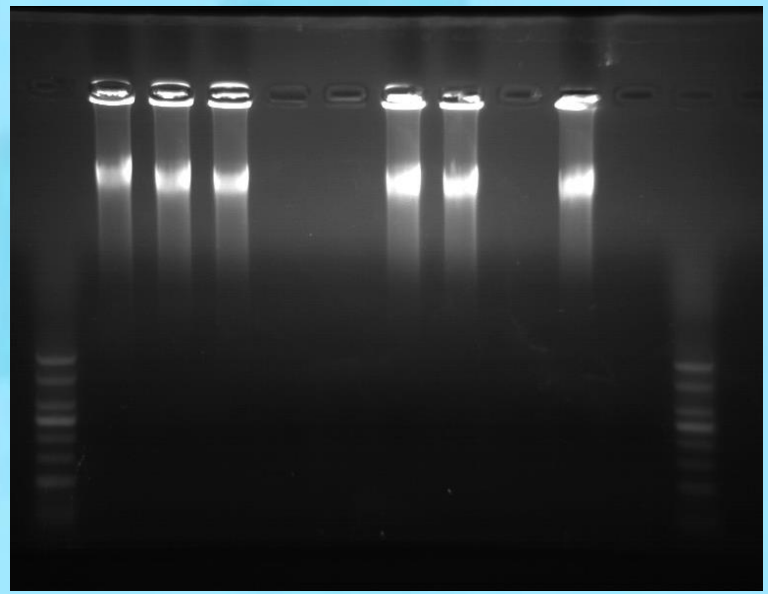
Gel electrophoresis

Date: 95.12.21

Test: GE Health Single Cell 2006 protocol

L 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

L: ladder
1- E1
2- E2
3- E3
4- E4
5- E5
6- E6
7- E7
8- E8
9- E9
10- ctrl-
11- L
12-
13-
14-
15-



Done by:

Checked by:

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First optimized PCR

Gel electrophoresis

Date: 96.1.15 Test: HBBN1R3R

L	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○

L: ladder 50bp

1- E1
2- E2
3- E3
4- E6
5- E7
6- E9
7-
8-
9-
10-
11-
12-

Done by:

96.1.15

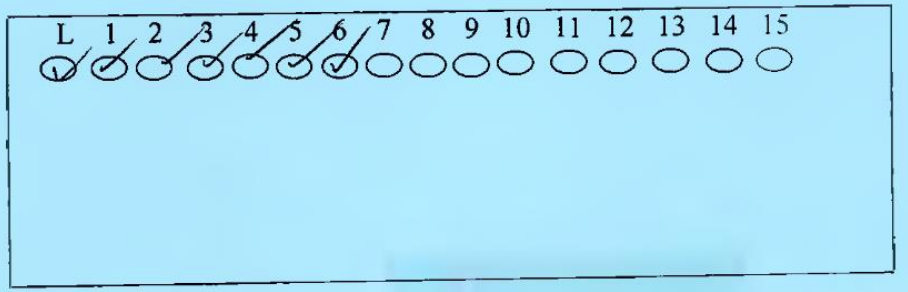
Checked by:

Second optimized PCR

Gel electrophoresis

Date: 96.2.9

Test HBBN1.FN1R



L: ladder

1- E_2

2- E_3

3- E_6

4- E_7

5- Leyla Shahbazi

6- Ctrl-

7-

8-

9-

10-

11-

12-

13-

14-

15-

Done by: Barati

Checked by: Jafari – Rezvani

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۹۶، ۲، ۹

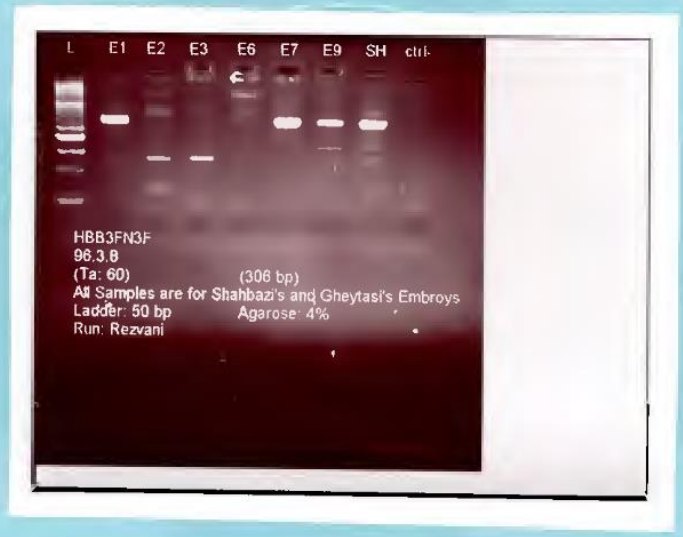
Third optimized PCR

Gel electrophoresis

Date: 96.3.8 Test: HBB3FN3F

L 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

L: ladder
1- E1
2- E2
3- E3
4- E6
5- E7
6- E9
7- Sh
8- ctrl-
9-
10-
11-
12-
13-
14-
15-



E1, E7, E9 مثبت

Done by:

Checked by:

Barad 96.3.8

96.3.8

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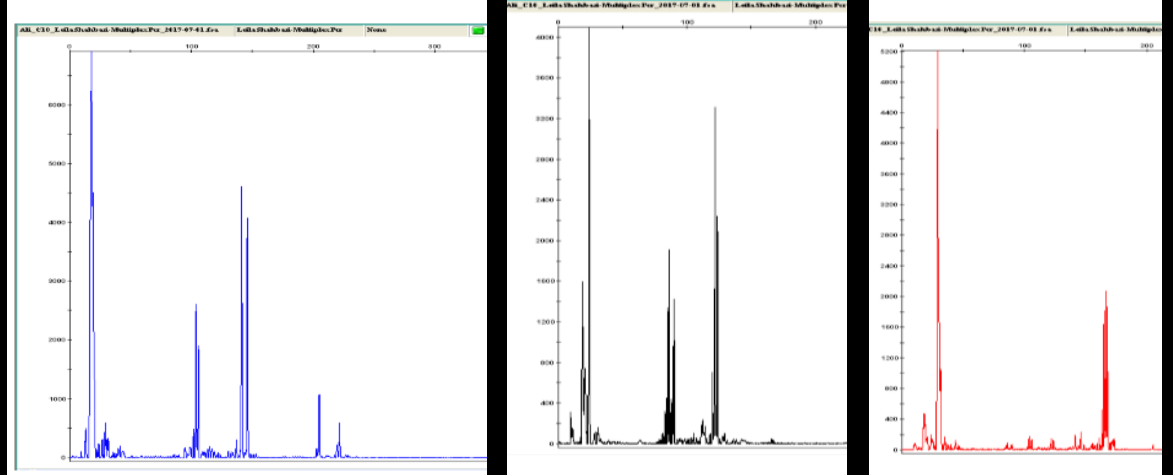
E1

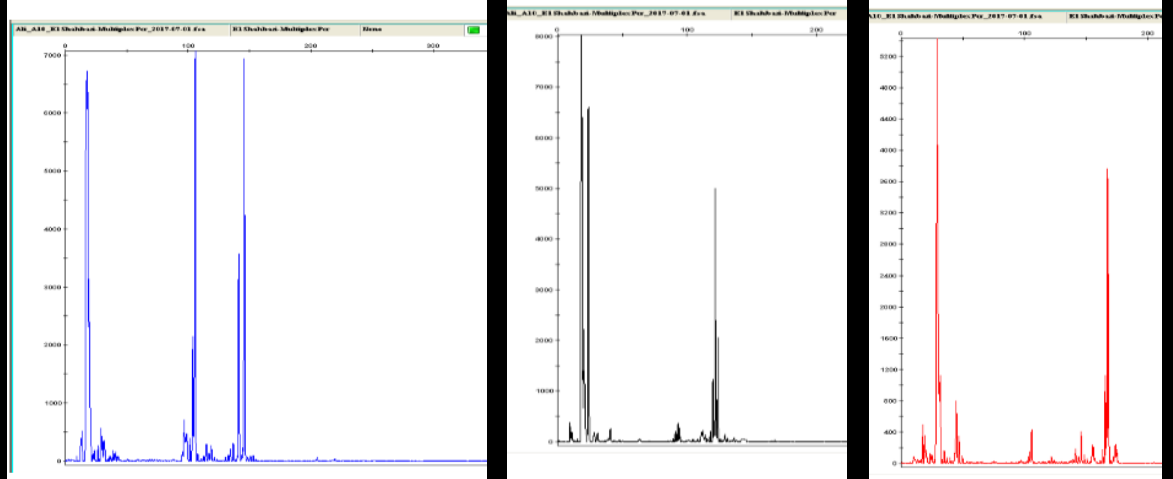
Rule out of contamination

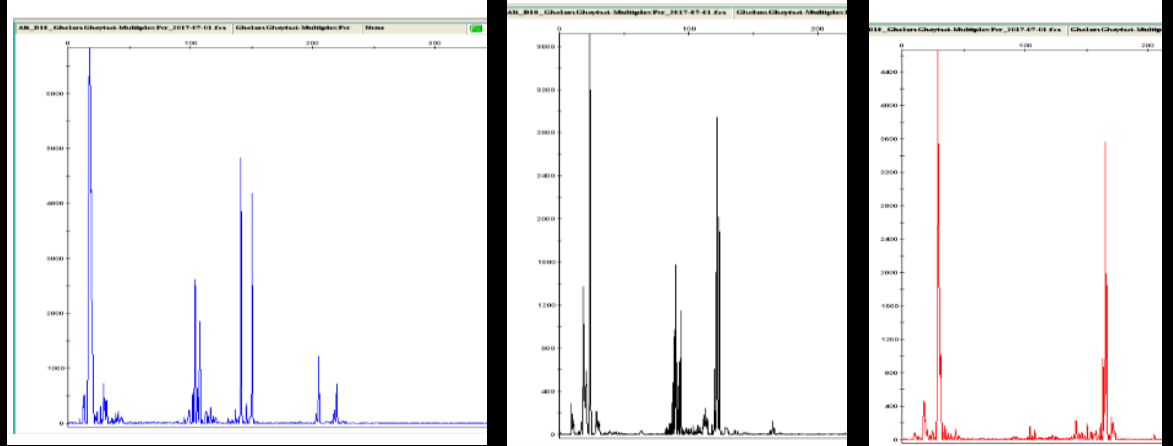
Mother

E1

Father







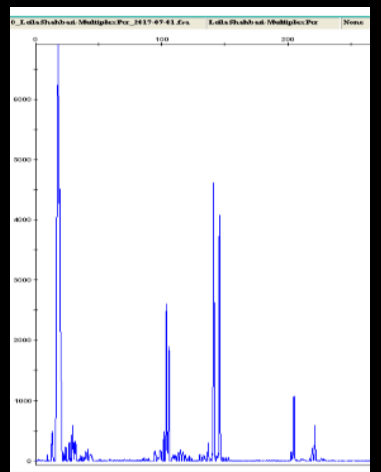
E7

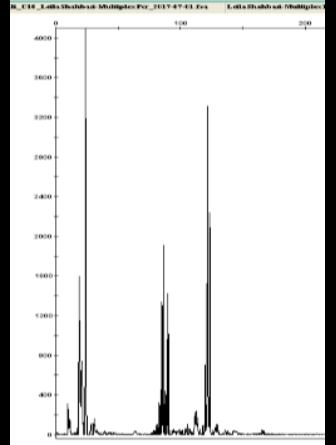
Rule out of contamination

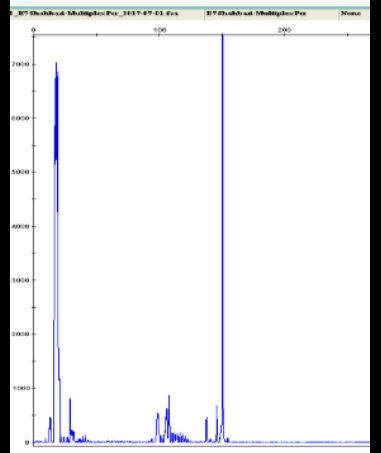
Mother

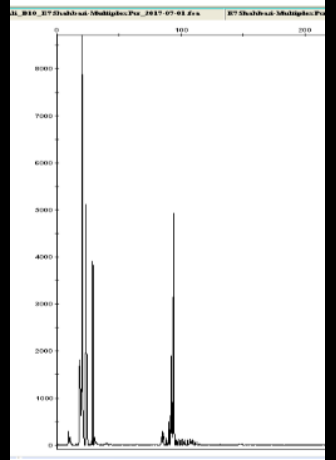
E1

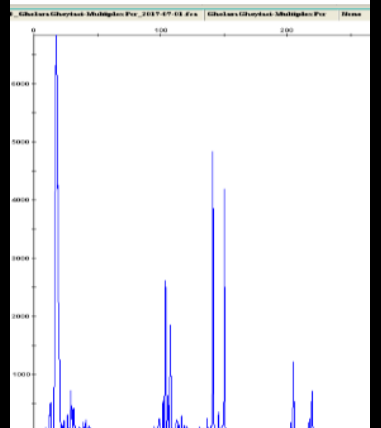
Father

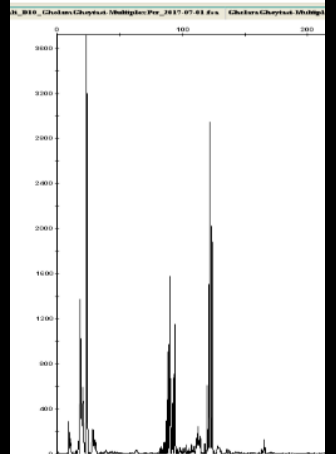












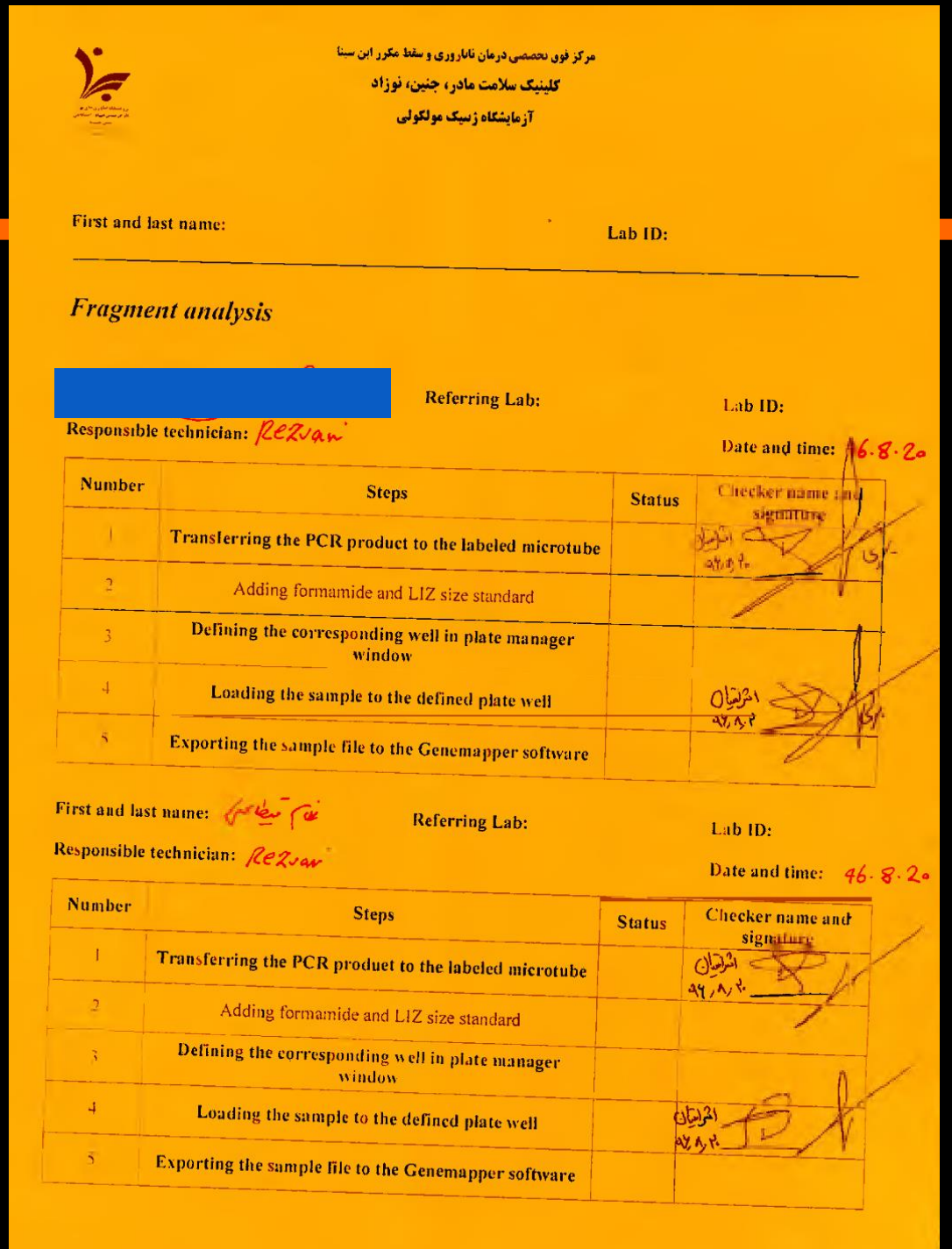
Summary of results

ID	HBB1	HBB2	HBB3	Final Result
E1	Normal Heterozygous	Normal Heterozygous	Normal Heterozygous	قابل انتقال
E37	Normal	Normal	Normal	قابل انتقال
E9	Mutated Homozygous	Mutated Homozygous	Mutated Homozygous	غيرقابل انتقال

Embryo Transfer

- Tow unaffected embryos (E1 and E7) were transferred (Mordad 1396, Aug 2017)
- The mother got pregnant (singleton pregnancy), and prenatal diagnosis was carried out on Aban 1396, Oct 2017

PND, Checklists



مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا
کلینیک سلامت مادر، جنین، نوزاد
آزمایشگاه ژنتیک مولکولی

First and last name: Lab ID:

Fragment analysis

[redacted] Referring Lab: Lab ID:

Responsible technician: Rezvan Date and time: 16.8.20

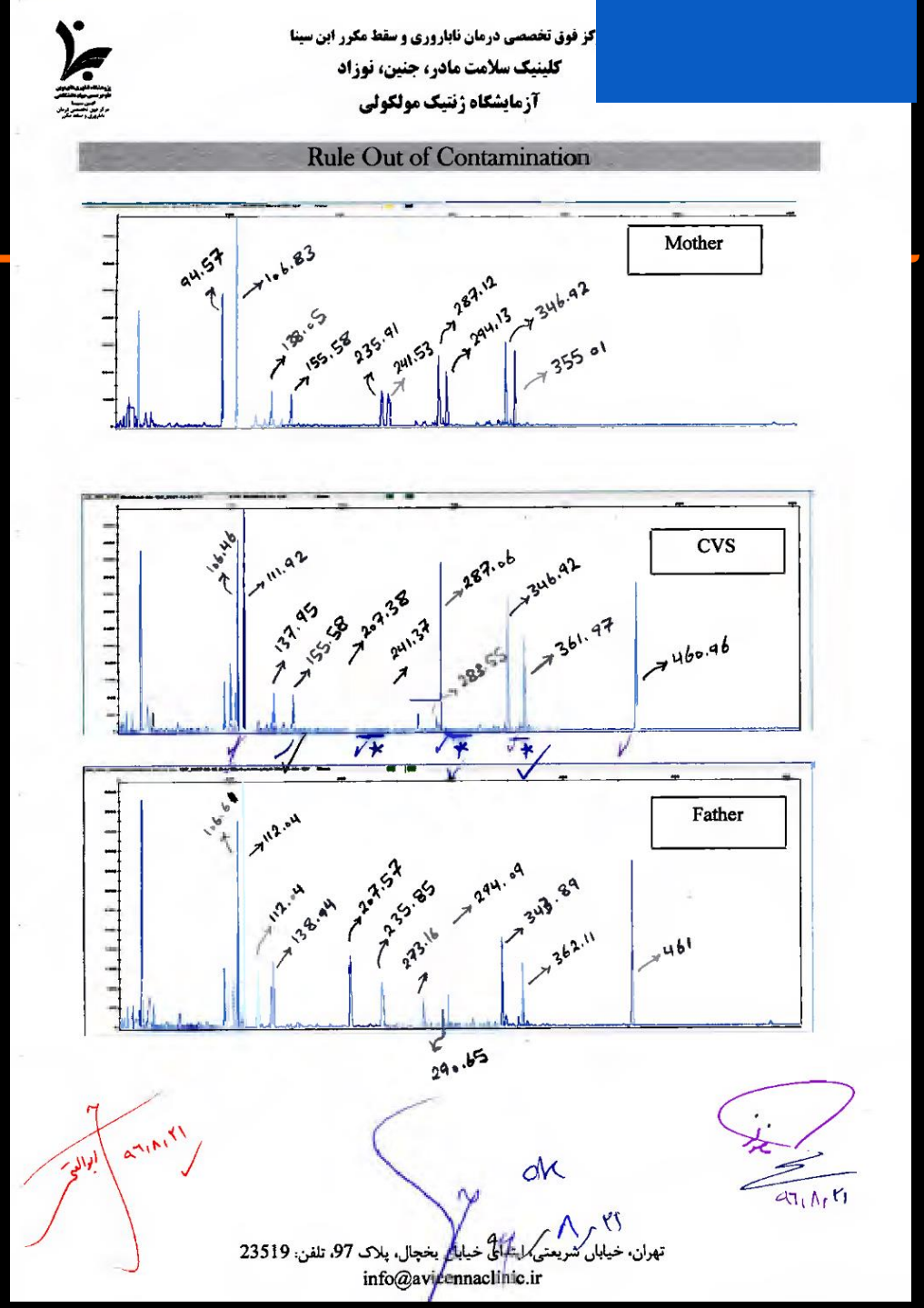
Number	Steps	Status	Checker name and signature
1	Transferring the PCR product to the labeled microtube		
2	Adding formamide and LIZ size standard		
3	Defining the corresponding well in plate manager window		
4	Loading the sample to the defined plate well		
5	Exporting the sample file to the Genemapper software		

First and last name: Referring Lab: Lab ID:

Responsible technician: Rezvan Date and time: 16.8.20

Number	Steps	Status	Checker name and signature
1	Transferring the PCR product to the labeled microtube		
2	Adding formamide and LIZ size standard		
3	Defining the corresponding well in plate manager window		
4	Loading the sample to the defined plate well		
5	Exporting the sample file to the Genemapper software		

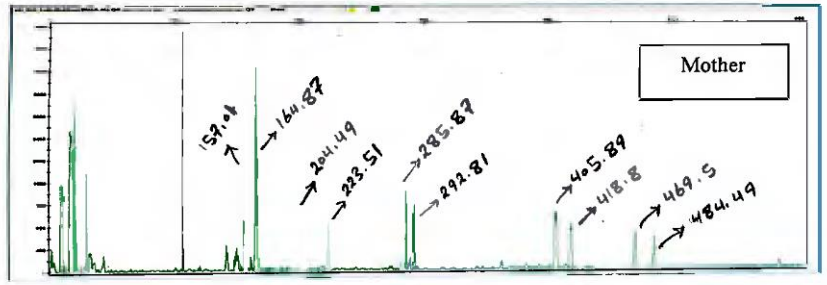
Rule out of maternal contamination

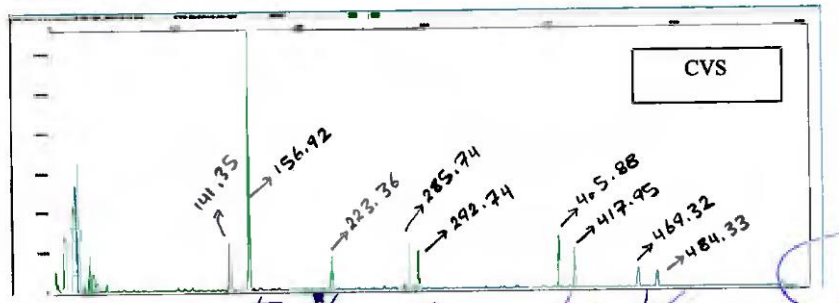


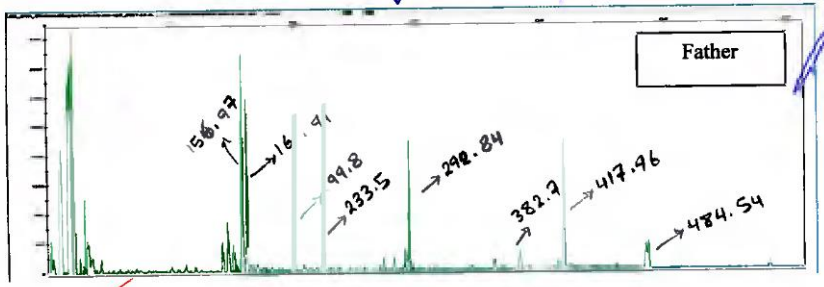
Rule out of maternal contamination

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا
کلینیک سلامت مادر، جنین، نوزاد
آزمایشگاه ژنتیک مولکولی

Rule Out of Contamination





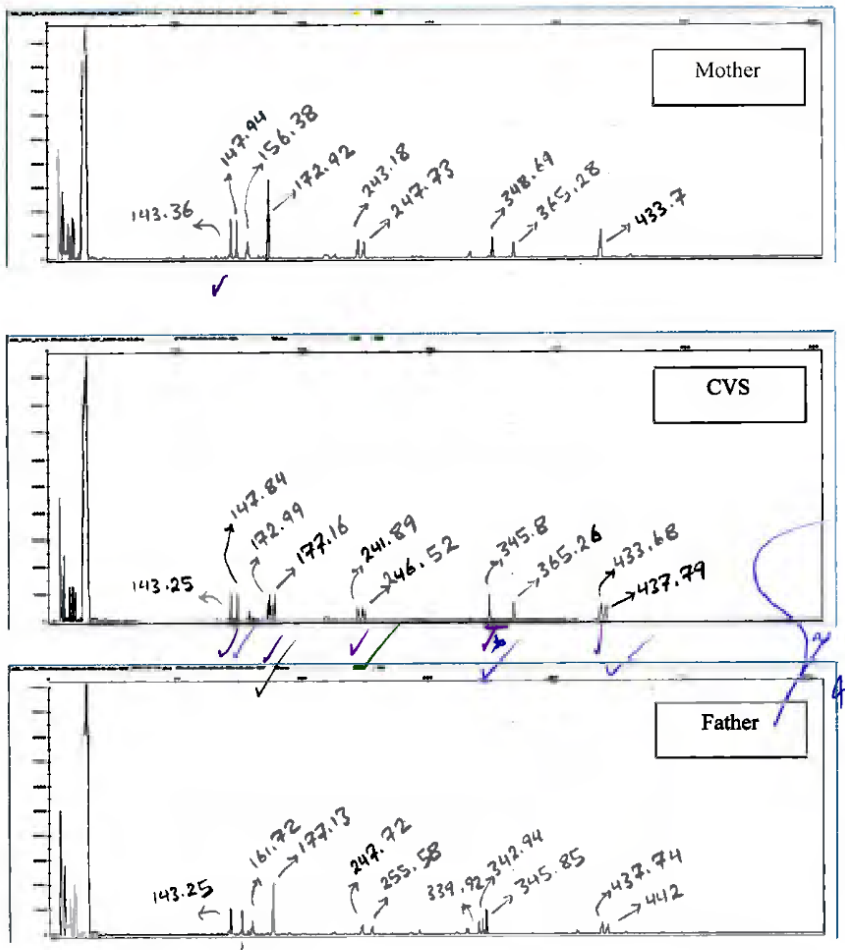


تهران، خیابان شریعتی، ابتدای خیابان یخچال، پلاک 97، تلفن: 23519
info@avicennaclinic.ir

Rule out of maternal contamination

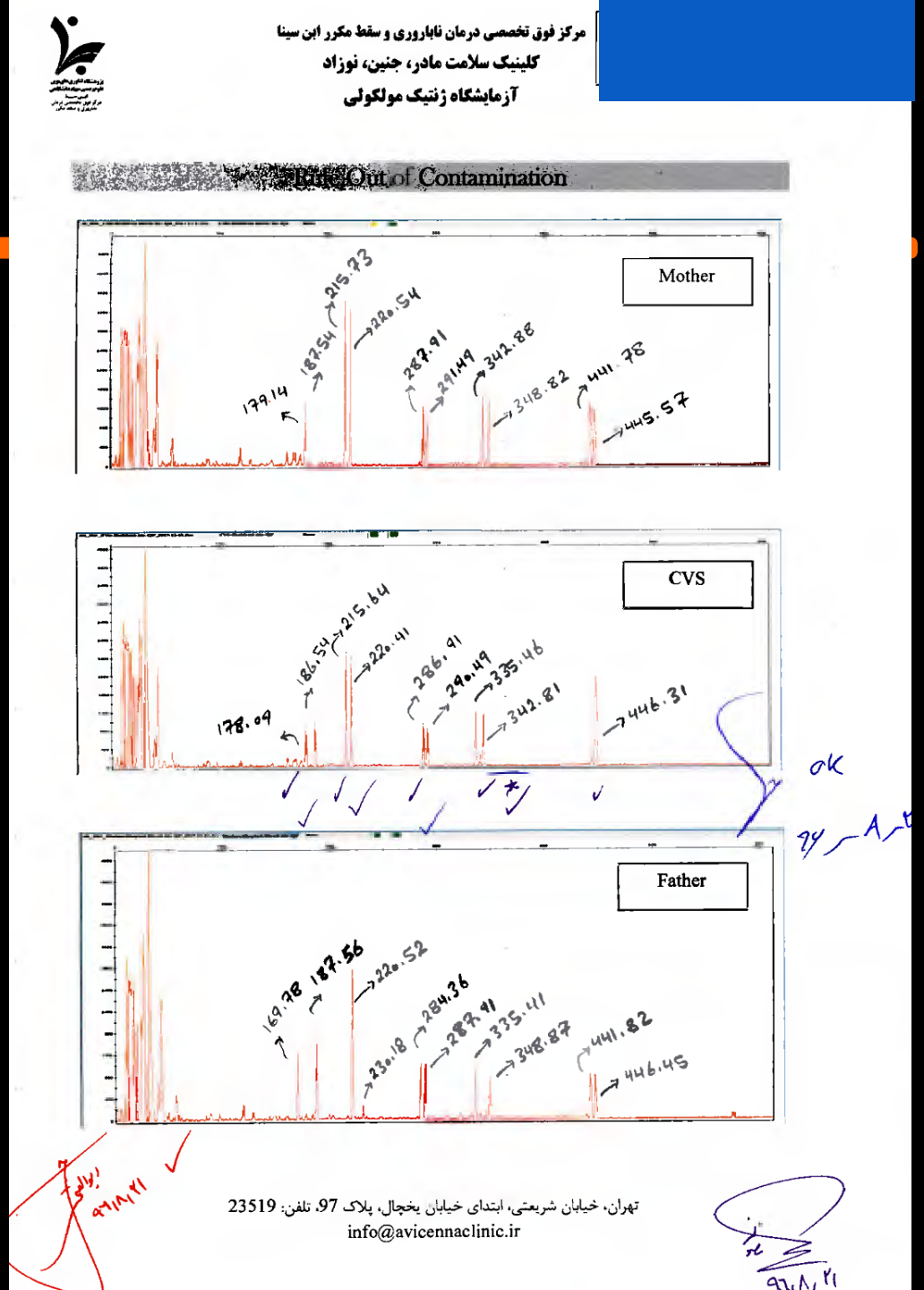
مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا
کلینیک سلامت مادر، جنین، نوزاد
آزمایشگاه ژنتیک مولکولی

Rule Out of Contamination



تهران، خیابان شریعتی، ابتدای خیابان یخچال، پلاک 97، تلفن: 23519
info@avicennaclinic.ir

Rule out of maternal contamination



مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا
کلینیک سلامت مادر، جنین، نوزاد
آزمایشگاه ژنتیک مولکولی

Rule Out of Contamination

Mother

179.14 187.54 215.73 220.54 287.91 291.49 342.88 348.82 441.78 445.57

CVS

178.09 186.54 215.64 220.41 286.91 290.49 335.46 342.81 446.31

ok

Father

169.38 187.56 220.52 230.18 284.36 287.91 335.41 348.87 441.82 446.45

تهران، خیابان شریعتی، ابتدای خیابان یخچال، پلاک 97، تلفن: 23519
info@avicennaclinic.ir

PND
CVS, Blind Test 1

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Gel electrophoresis

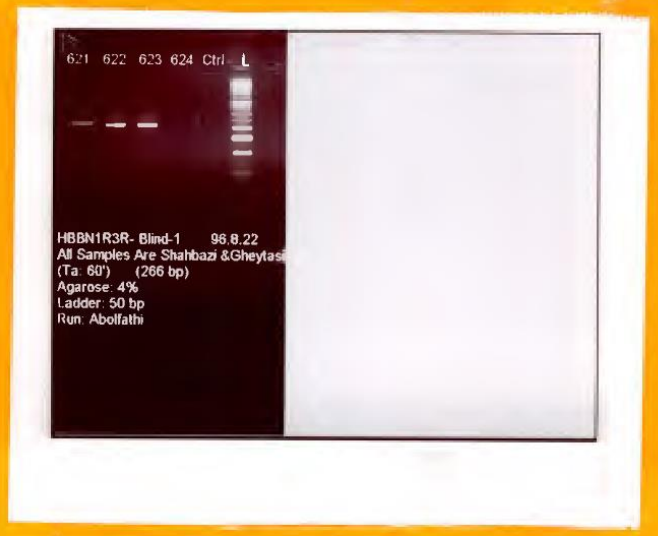
L 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

Blind1 _ HBBN1R-3R

96.8.22

L: ladder

1-
2-
3-
4-
5-
6-
7-
8-
9-
10-
11-
12-
13-
14-
15-



Done by:

Checked by:

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا
کلینیک سلامت مادر، جنین، نوزاد
آزمایشگاه ژنتیک مولکولی

BLIND TEST

Date: 96.8.22 Test: HBBN1R3R

[redacted]

Code	Sample	Status	Checked By:
621	Mahdiyeh Ahmadi (Ctrl Normal)		
622	CVS Shahbazi		
623	Gholam Gheytasi (Heterozygote Ctrl)		
624	Ctrl -		

Done By:

Checked By:

Normal CTRL

مرکز فوق تخصصی درمان ناباروری و سلول مادر ابن سینا

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Mutation Detection

Beta Thalassemia

Blind-1

Sample ID: 621
Mother's and Father's Mutation: c.112delT
PCR Date: 1396.08.22
Sequencing Date: 1396.08.23

Sampling Date: 1396.08.18
Primer Set: HBBN1R3R
Primer Set: HBBN1R

Wild Type Sequence:

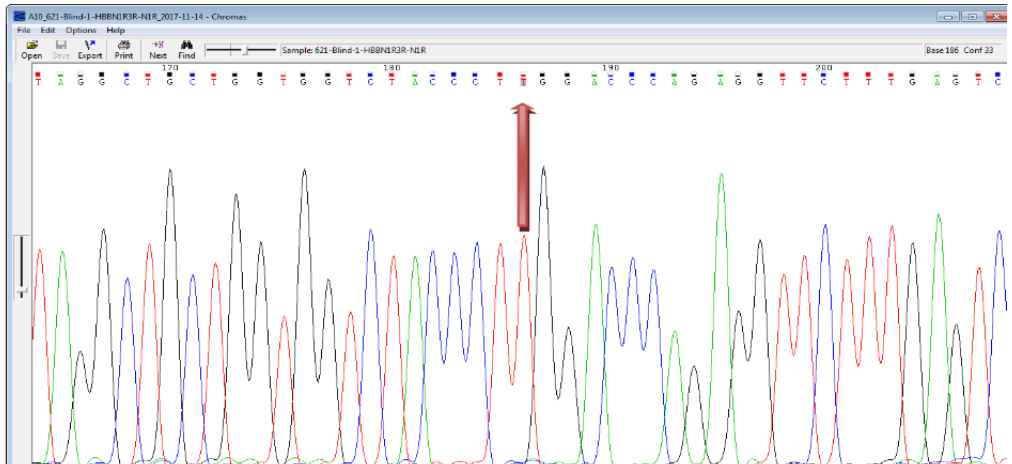
AGAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCAAGG
TTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGCACTGACTC
TCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGATCT
GTCCACTCCTGA

Wild Type

>621-Blind-1-HBBN1R3R-N1R sequence exported from A10_621-Blind-1-HBBN1R3R-N1R_2017-11-14.ab1

NNNNNNNNNNNNNNNTNGNGGTGNNGCCCTGGGCNGGTTGGTNTCAAGGTTNNAAGANAGGTTTAAGGNNACCAATANA
AACTGGGCATGTGGANACAGANAANANTCTTGGGTTTCTGATAGGCACTGACTCTCTCTGCCTATTGGTCTATTTTCCC
ACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGNNNNNNNNCNNNNNCCTGAA

Wild Type



CVS, Normal

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Mutation Detection

Beta Thalassemia

Blind-1

Sample ID: 622
Mother's and Father's Mutation: c.112delT
PCR Date: 1396.08.22
Sequencing Date: 1396.08.23

Sampling Date: 1396.08.18
Primer Set: HBBN1R3R
Primer Set: HBBN1R

Wild Type Sequence:

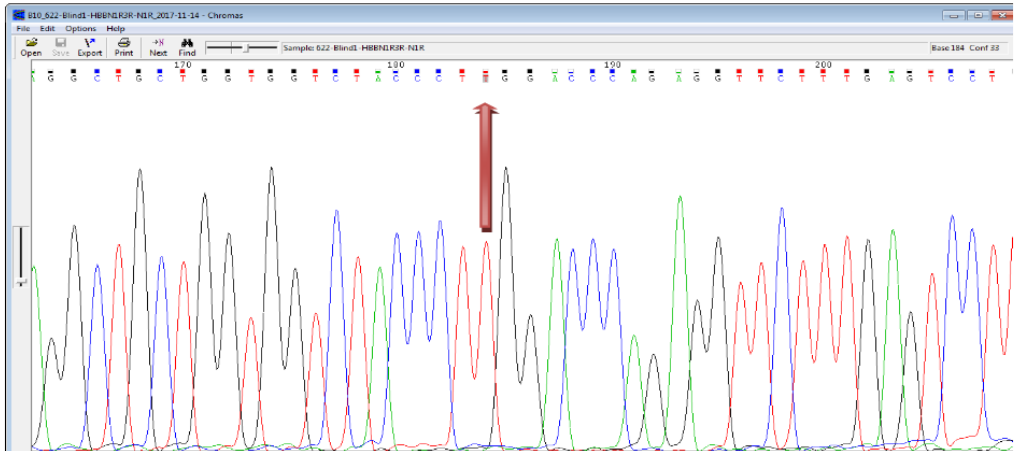
AGAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCAAGG
TTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGCACTGACTC
TCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGATCT
GTCCACTCCTGA

Wild Type

>>622-Blind1-HBBN1R3R-N1R sequence exported from B10_622-Blind1-HBBN1R3R-N1R_2017-11-14.ab1

NNNNNNNNNNNNNNTNGTGGTGNNGCCCTGGGCNGGTTGGTNTCANGGTTNCAAGACAGGTTTAAGGANNNCAATAGAAA
CTGGGCATGTGGAGACAGANAAGANTCTTGGGTTTCTGATAGGCACTGACTCTCTCTGCCTATTGGTCTATTTTCCCAC
CCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGNNNNNNNCNCNNNCCTGAAAANNN

Wild Type



Carrier, CTRL

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Mutation Detection

Beta Thalassemia

Blind-1

Sample ID: 623
Mother's and Father's Mutation: c.112delT
PCR Date: 1396.08.22
Sequencing Date: 1396.08.23

Sampling Date: 1396.08.18
Primer Set: HBBN1R3R
Primer Set: HBBN1R

Wild Type Sequence:

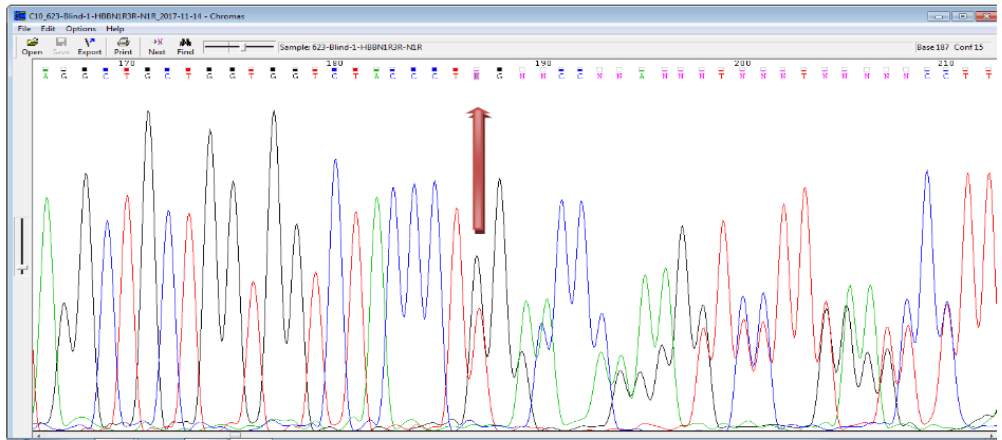
AGAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCAAGG
TTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGCACTGACTC
TCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGATCT
GTCCACTCCTGA

Wild Type

>623-Blind-1-HBBN1R3R-N1R sequence exported from C10_623-Blind-1-HBBN1R3R-N1R_2017-11-14.ab1

NNNNNNNNNNNNNNNNNTNNNGNNGNNGCNNGGGCANGNNGGTNNCANGNNNTNCAAGANAGGTTTAAGGANACCAATAN
AAACTGGGCNTGTGGANACAGANAANANTCTTGGGTTTCTGANAGGCACTGACTCTCTCTGCCTATTGGTCTATTTTCC
CACCCTTAGGCTGCTGGTGGTCTACCCTKGNNCCNNANNNTNNNTNNNNNCCTTNGNGNNNNNNCCNNNNCNNNNNNAN
NGTACNNNNNNNAANNNNNNNNNNNNNNTGNA

Heterozygous



PND
CVS, Blind Test 2

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Gel electrophoresis

Test: HBBN1R3R *Date* 96.8.24

L 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

L: ladder

1-
2-
3-
4-
5-
6-
7-
8-
9-
10-

Done by:

Checked by:

96.8.24

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا
کلینیک سلامت مادر، جنین، نوزاد
آزمایشگاه ژنتیک مولکولی

BLIND TEST

Date: 96.8.24 **Test: HBBN1R3R**

[redacted]

Code	Sample	Status	Checked By:
625	Mahdiyeh Ahmadi (Ctrl Normal)		
626	CVS Shahbazi		
627	Ctrl -		
628	E9 (Affected Ctrl)		
629	CVS Shahbazi		
630	Gholam Gheytasi (Heterozygote Ctrl)		

Done By: Dr Rafati

Checked By:

CVS, Normal

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Mutation Detection

Beta Thalassemia

Blind-2

Sample ID: 625
Mother's and Father's Mutation: c.112delT
PCR Date: 1396.08.24
Sequencing Date: 1396.08.29

Sampling Date: 1396.08.18
Primer Set: HBBN1R3R
Primer Set: HBBN1R

Wild Type Sequence:

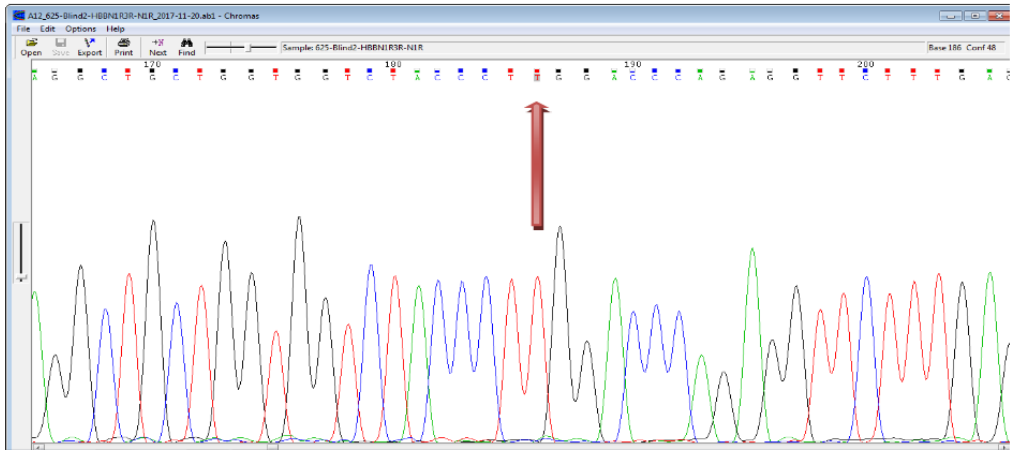
AGAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCAAGG
TTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGCACTGACTC
TCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGATCT
GTCCACTCCTGA

Wild Type

>625-Blind2-HBBN1R3R-N1R sequence exported from A12_625-Blind2-HBBN1R3R-N1R_2017-11-20.ab1

NNNNNNNNNNNNNNNNTNGTGGTGNNGCCCTGGGCANGTTGGTNTCAAGGTTNCAAGACAGGTTTAAGGNNNNCAATAGA
AACTGGGCATGTGGAGACAGANAAGNNTCTTGGGTTTCTGATAGGCACTGACTCTCTCTGCCTATTGGTCTATTTTCCC
ACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGNNNNNNNGNNCCNCTCCTGAA

Normal



CVS, Normal

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Mutation Detection

Beta Thalassemia

Blind-2

Sample ID: 626
Mother's and Father's Mutation: c.112delT
PCR Date: 1396.08.24
Sequencing Date: 1396.08.29

Sampling Date: 1396.08.18
Primer Set: HBBN1R3R
Primer Set: HBBN1R

Wild Type Sequence:

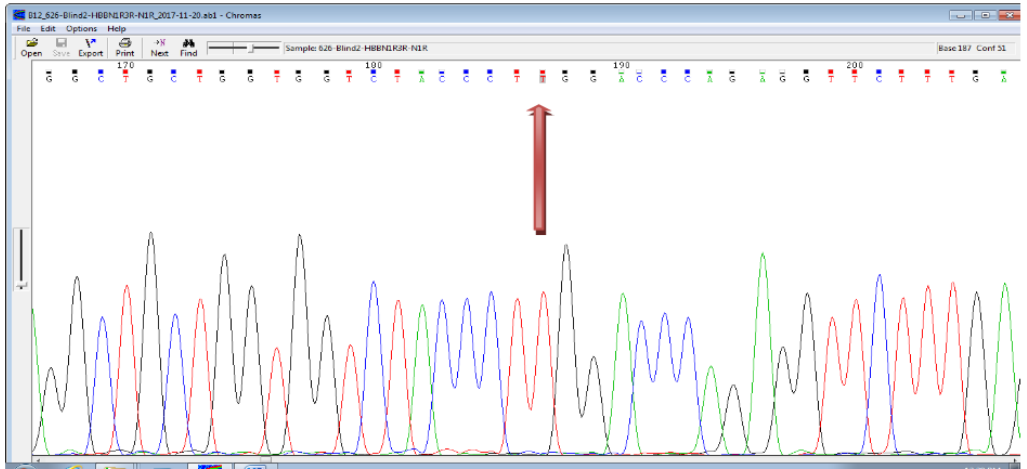
AGAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCAAGG
TTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGCACTGACTC
TCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGATCT
GTCCACTCCTGA

Wild Type

>626-Blind2-HBBN1R3R-N1R sequence exported from B12_626-Blind2-HBBN1R3R-N1R_2017-11-20.ab1

NNNNNNNNNNNNNNNNNGNGGTGNNGCNCTGGGCNNGTTGGTNTCAAGGTTACAAGACAGGTTTNNNNNNNNCCAATAG
AAACTGGGCATGTGGAGACAGAGAAGANTCTTGGGTTTCTGATAGGCACTGACTCTCTCTGCCTATTGGTCTATTTTCC
CACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGNNNNNNNCCNCTCCTGAA

Normal



Control
Affected, E9

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Mutation Detection

Beta Thalassemia

Blind-2

Sample ID: 628
Mother's and Father's Mutation: c.112delT
Sampling Date: 1396.08.18
PCR Date: 1396.08.24
Primer Set: HBBN1R3R
Sequencing Date: 1396.08.29
Primer Set: HBBN1R

Wild Type Sequence:

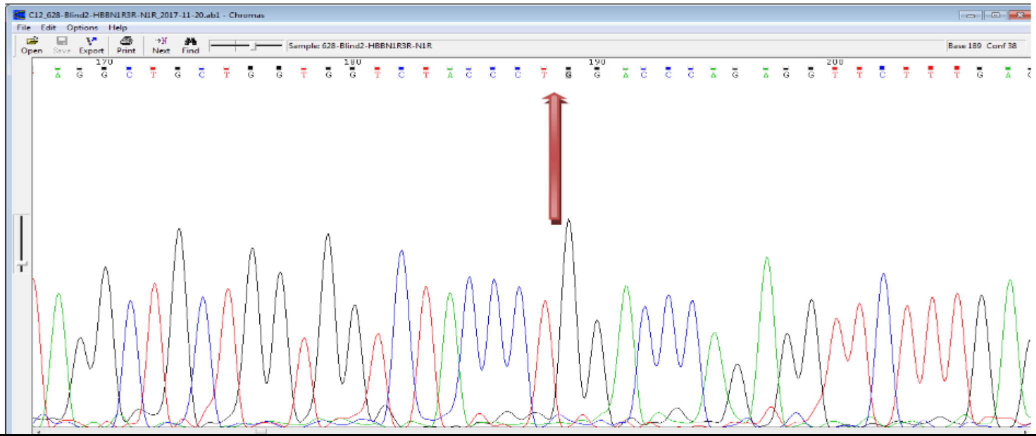
AGAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCAAGG
TTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGCACTGACTC
TCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGATCT
GTCCACTCCTGA

Wild Type

>628-Blind2-HBBN1R3R-N1R sequence exported from C12_628-Blind2-HBBN1R3R-N1R_2017-11-20.ab1

NNNNNNNNNNNNNNNNNNNNNNNNNNNNNCNNGNNNNNNGNNNNNNNCNNGNNNTNNNAGANAGGTTTNNNNNNNNNCAAT
ANNAACTGGGCATGTGGAGACAGANAAGACTCTTGGGTTTCTGATAGGCACTGACTCTCTCTGCCTATTGGTCTATTTT
CCCACCCTTAGGCTGCTGGTGGTCTACCCTGGACCCAGAGGTTCTTTGAGTCCTTTGGGNANCTNNCCCACTCCTGAAN
NCNNCNNGGGNTCTGTNNNCTCCTGAANN … NNTNNNNCNNTTNNNNNNNNNNGNNNNNNA
ANNTGAAAAAANNNNACTTNCNNNNNGNNAAG … NNANNGNNNGNTTTTGCNNNACTNNTNGCT

Homozygous



Carrier, control

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Mutation Detection

Beta Thalassemia

Blind-2

Sample ID: 630
Mother's and Father's Mutation: c.112delT
PCR Date: 1396.08.24
Sequencing Date: 1396.08.29

Sampling Date: 1396.08.18
Primer Set: HBBN1R3R
Primer Set: HBBN1R

Wild Type Sequence:

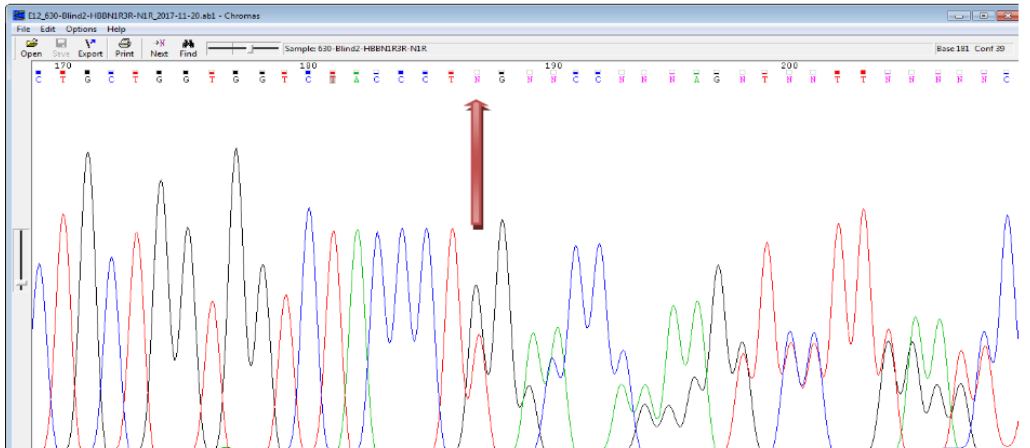
AGAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCAAGG
TTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGCACTGACTC
TCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGATCT
GTCCACTCCTGA

Wild Type

>630-Blind2-HBBN1R3R-N1R sequence exported from E12_630-Blind2-HBBN1R3R-N1R_2017-11-20.ab1

NNNNNNNNNNNNNNNNNTNNNGGTGANGCCCTGGGCAGGTTGGTNTCANGGNTACAAGANAGGTTTNNGGAGA
NCAATANAAACTGGGCATGTGGAGACAGANAAGANTCTTGGGTTTCTGATAGGCACTGACTCTCTCTGCCTA
TTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTNGNNCCNNNAGNTNNTTNNNNNCNNTNNNN
NNNNNNNCCNNNCCNNNNN

Heterozygous

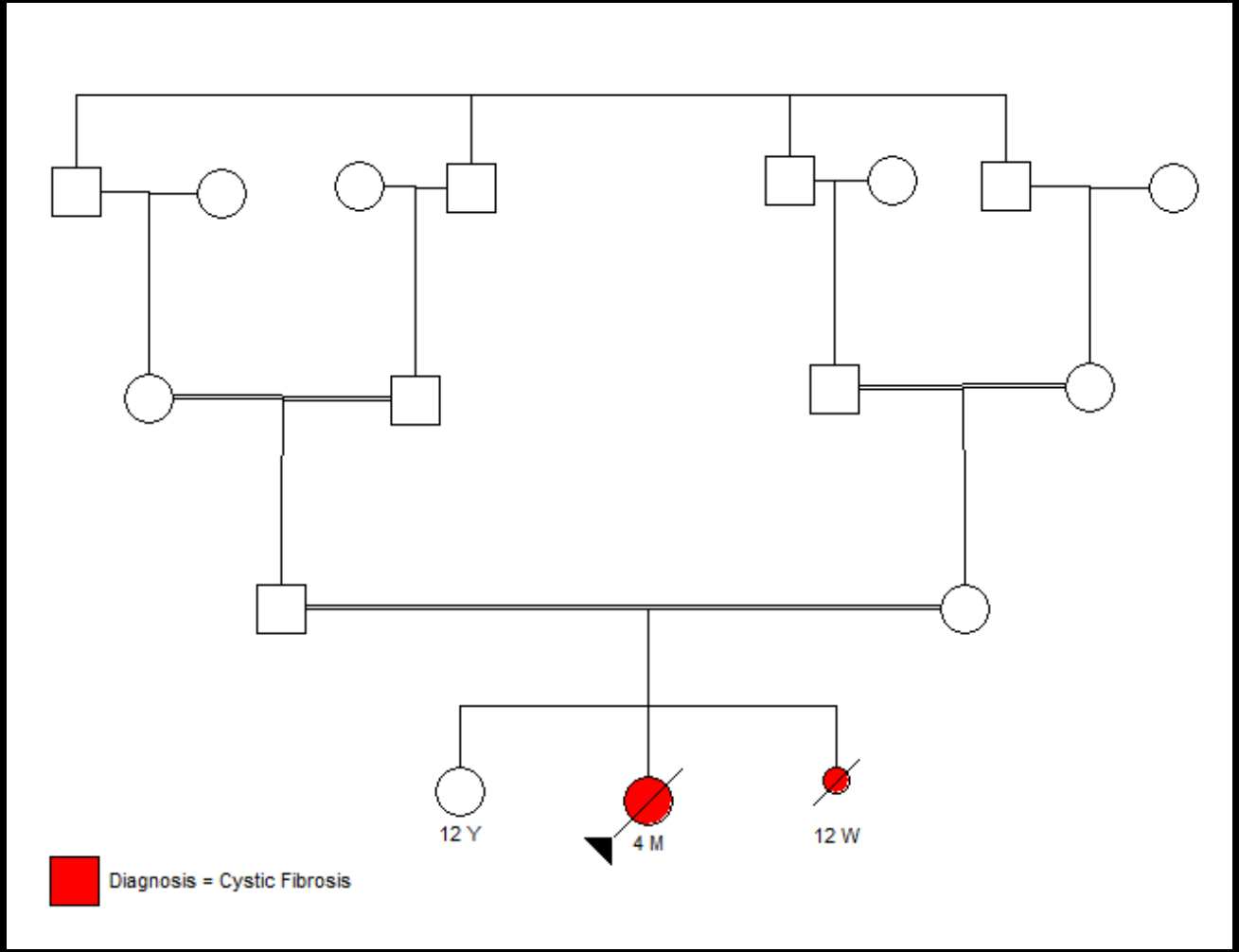


Final report

- The fetus was unaffected
- PND confirmed PGT-M results

Cystic Fibrosis

Pedigree

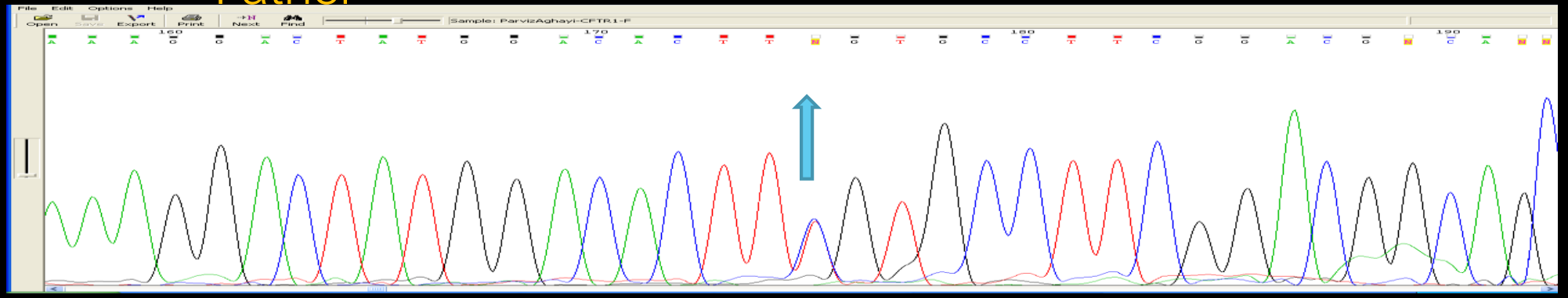


Mutation Detection

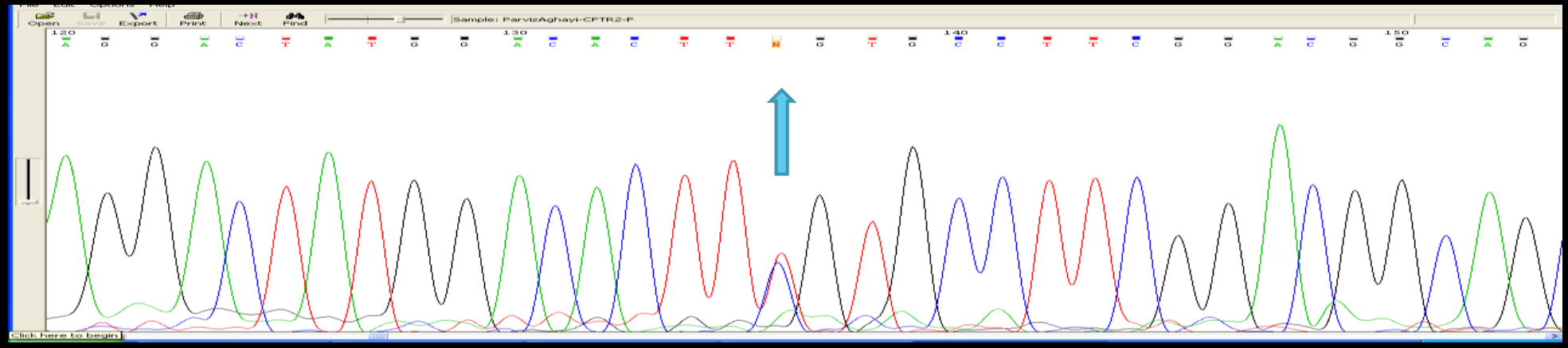
- Both parents:
  - Homozygous mutation in *CFTR* gene
  - C.3196C>T (R1066C)

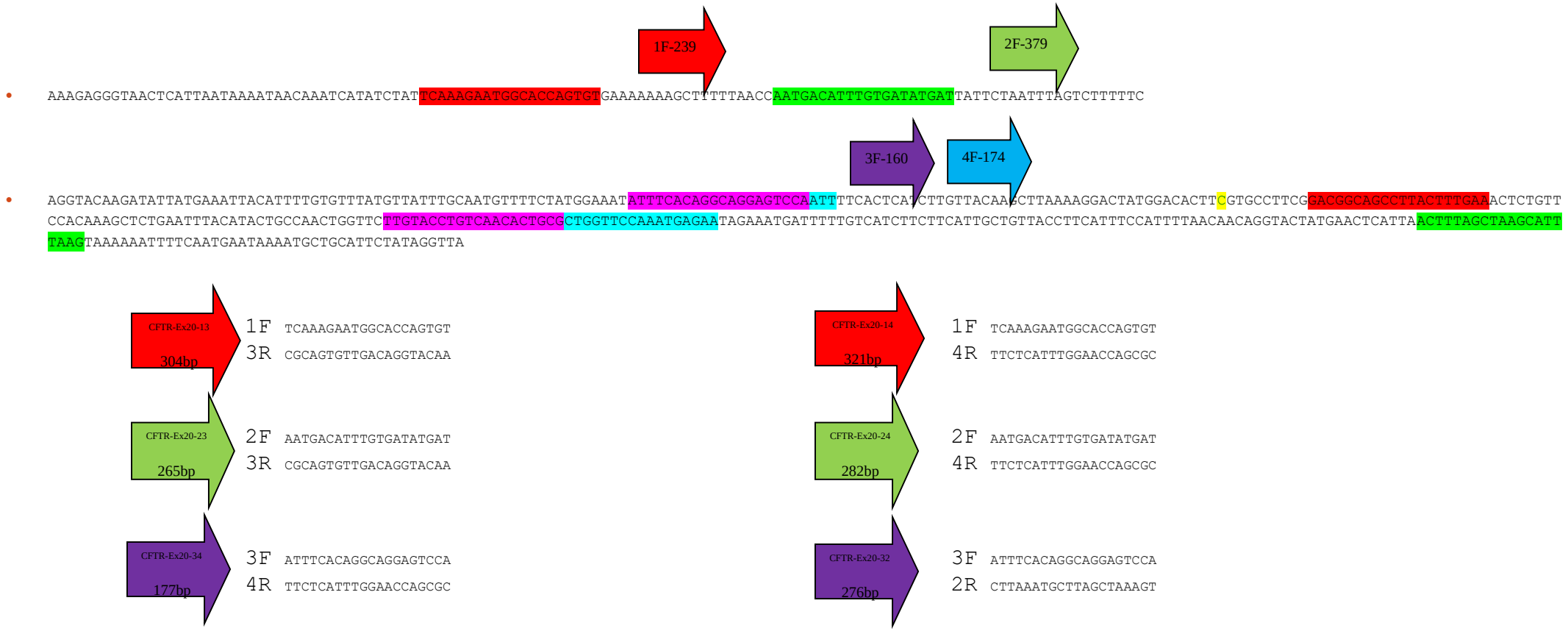
Mutation confirmation

Father

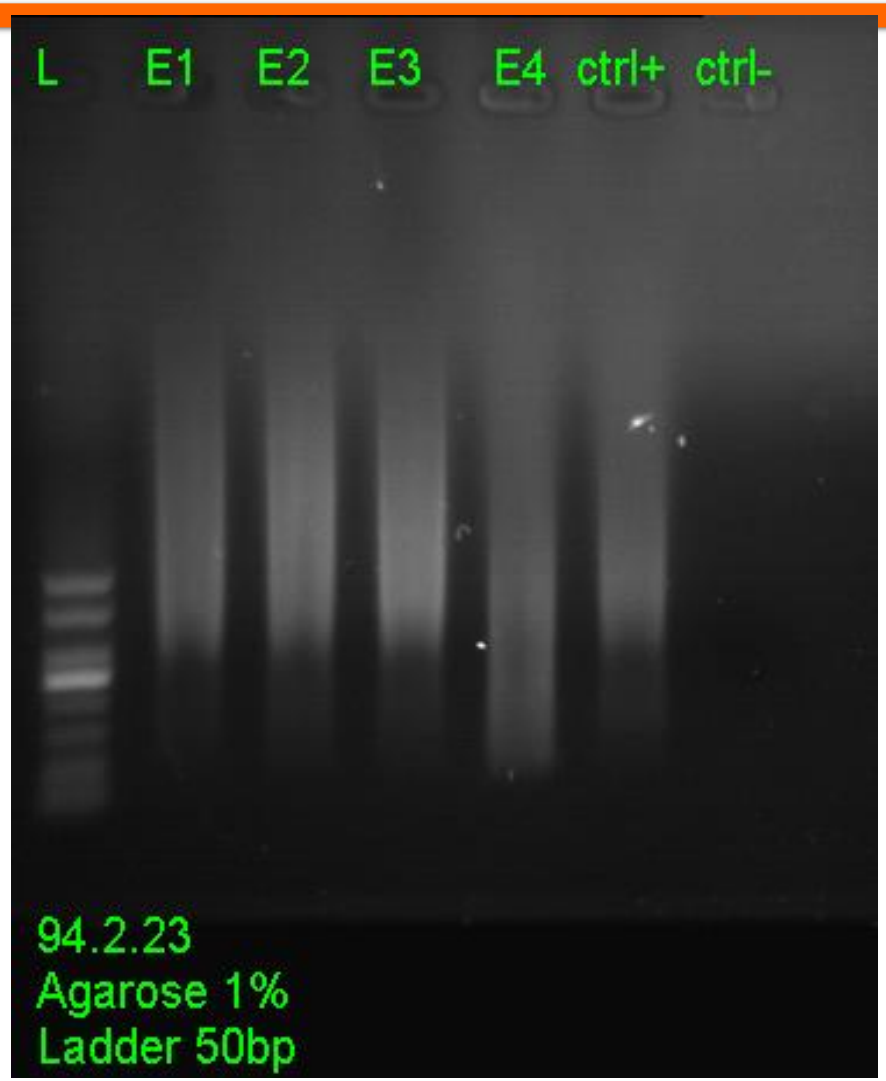


Mother




1F-239
2F-379
AAAGAGGGTAACTCATTAATAAAATAACAAATCATATCTATTCAAAGAATGGCACCAGTGTGAAAAAAAGCTTTTTAACCAATGACATTTGTGATATGATTATTCTAATTTAGTCTTTTTC
3F-160
4F-174
AGGTACAAGATATTATGAAATTACATTTTGTGTTTATGTTATTTGCAATGTTTTCTATGGAAATATTTCACAGGCAGGAGTCCAATTTTCACTCATCTTGTTACAAGCTTAAAAGGACTATGGACACTTCGTGCCTTCGGACGGCAGCCTTACTTTGAAACTCTGTT
CCACAAAGCTCTGAATTTACATACTGCCAACTGGTTCTTGTACCTGTCAACACTGCGCTGGTTCCAAATGAGAATAGAAATGATTTTTGTCATCTTCTTCATTGCTGTTACCTTCATTTCCATTTTAACAACAGGTACTATGAACTCATTAACTTTAGCTAAGCATT
TAAGTAAAAAATTTTCAATGAATAAAATGCTGCATTCTATAGGTTA
CFTR-Ex20-13
304bp
1F TCAAAGAATGGCACCAGTGT
3R CGCAGTGTTGACAGGTACAA
CFTR-Ex20-14
321bp
1F TCAAAGAATGGCACCAGTGT
4R TTCTCATTTGGAACCAGCGC
CFTR-Ex20-23
265bp
2F AATGACATTTGTGATATGAT
3R CGCAGTGTTGACAGGTACAA
CFTR-Ex20-24
282bp
2F AATGACATTTGTGATATGAT
4R TTCTCATTTGGAACCAGCGC
CFTR-Ex20-34
177bp
3F ATTTCACAGGCAGGAGTCCA
4R TTCTCATTTGGAACCAGCGC
CFTR-Ex20-32
276bp
3F ATTTCACAGGCAGGAGTCCA
2R CTTAAATGCTTAGCTAAAGT

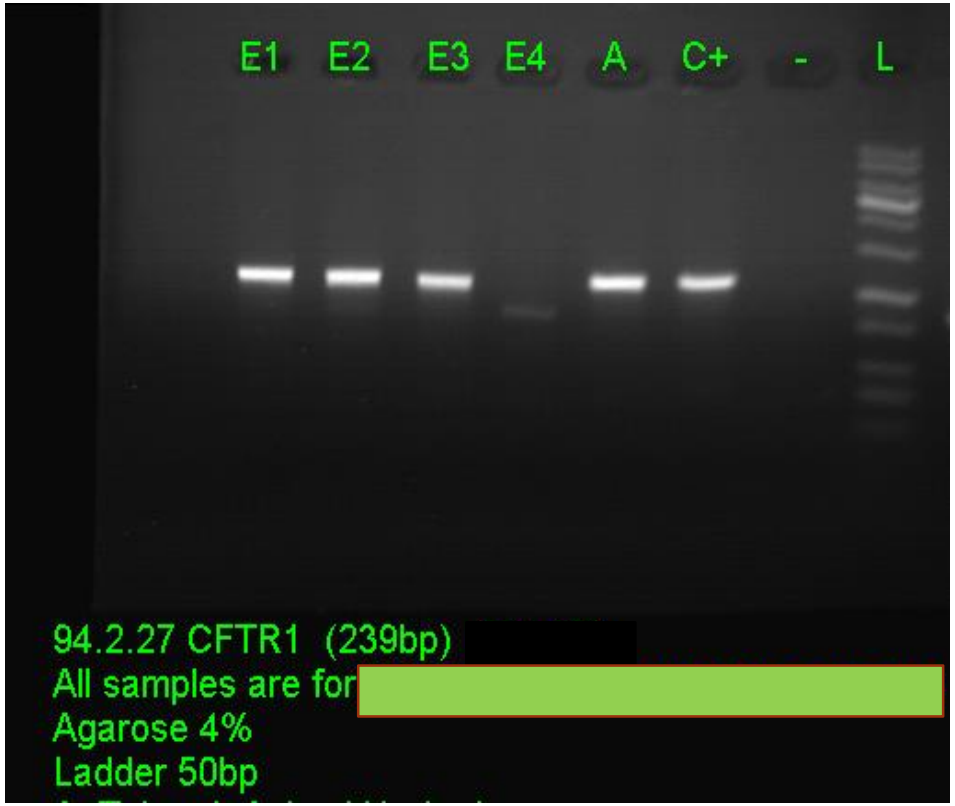
Single-cell Whole Genome Amplification
Assessment of DNA quality

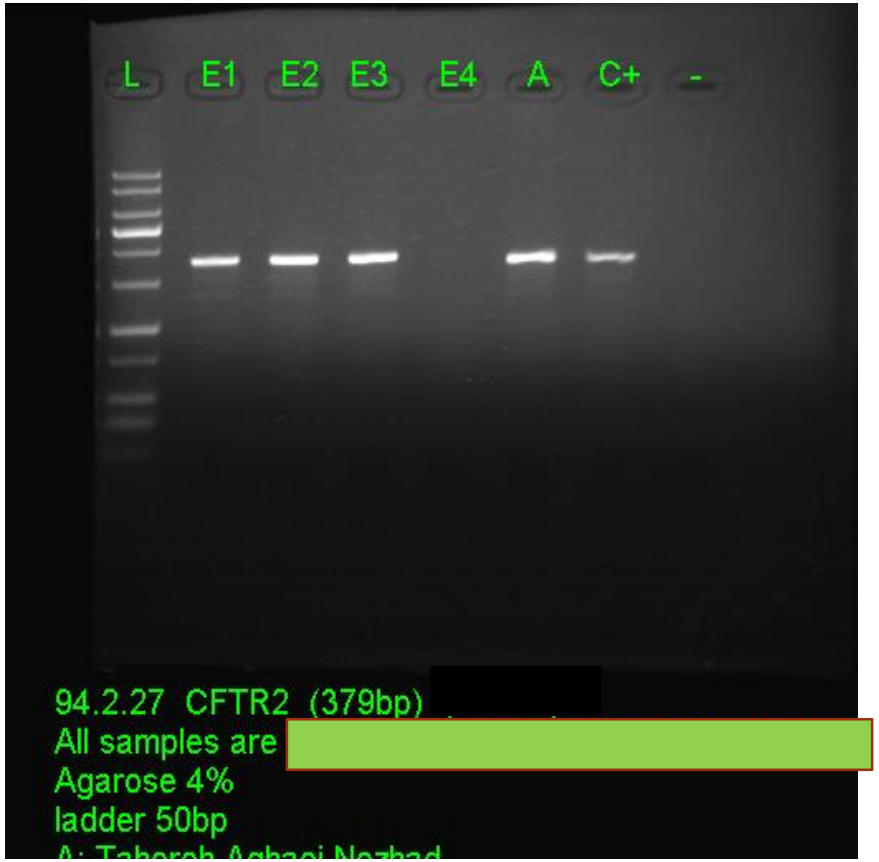


Single-cell Whole Genome Amplification
Assessment of DNA quality and quantity

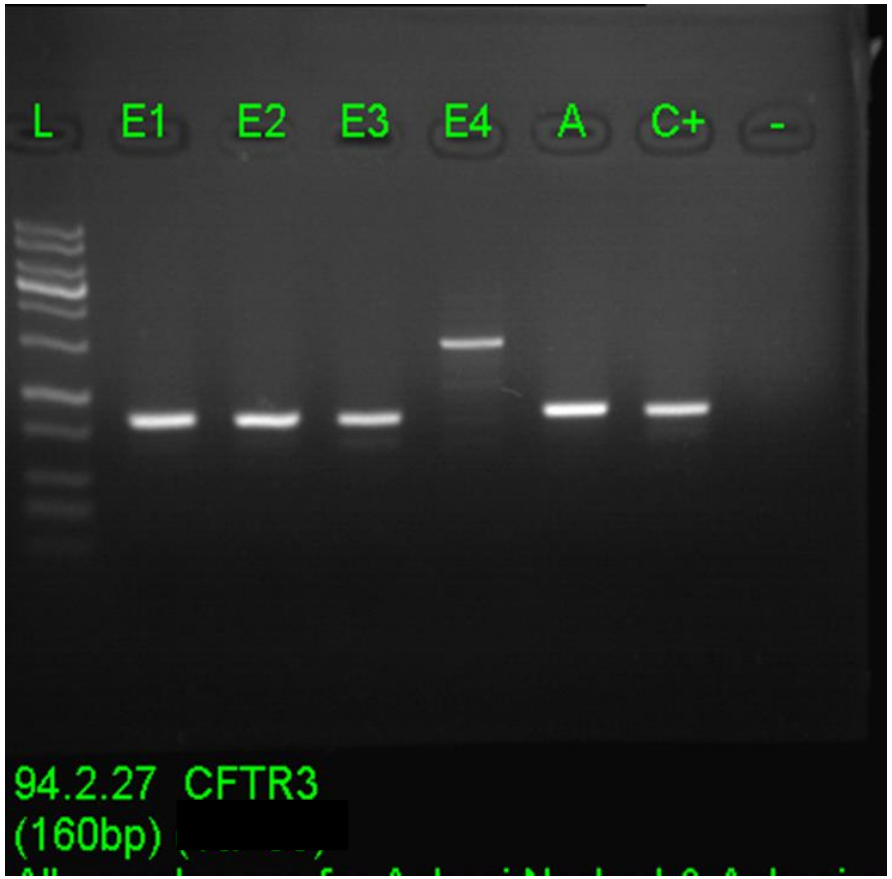
Embryo's ID	Concentration ng/µl	260/280	260/230
E1(3Cell)	290.9	1.9	2.21
E2(2Cell)	259.8	1.89	2.31
E3(2Cell)	270.5	1.91	2.31
E4(2Cell)	195.4	1.88	2.38
Ctrl+	190.3	1.9	1.99
Ctrl-	8.7	1.59	1.52

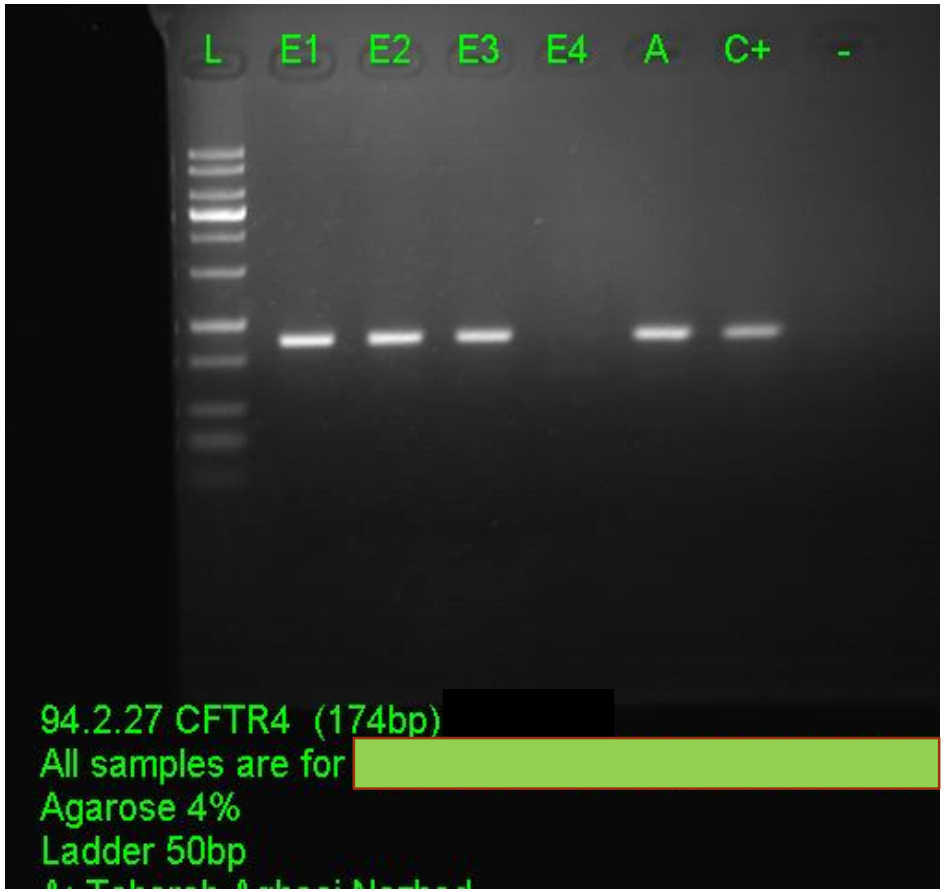
Amplification of Specific Targets





Amplification of Specific Targets





Embryo 1, CFTR1, Heterozygous (carrier)

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کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Preimplantation Genetic Diagnosis

Cystic Fibrosis

E1 (Heterozygous Normal)

Embryos ID: E1
Mutation: c.3196C>T (R1066C)
PCR Date: 1394.02.27
Sequencing Date: 1394.02.29

Parents: [redacted]
Sampling Date: 1394.02.23
Primer Set: CFTR1
Primer Set: CFTR1F

Wild Type Sequence:

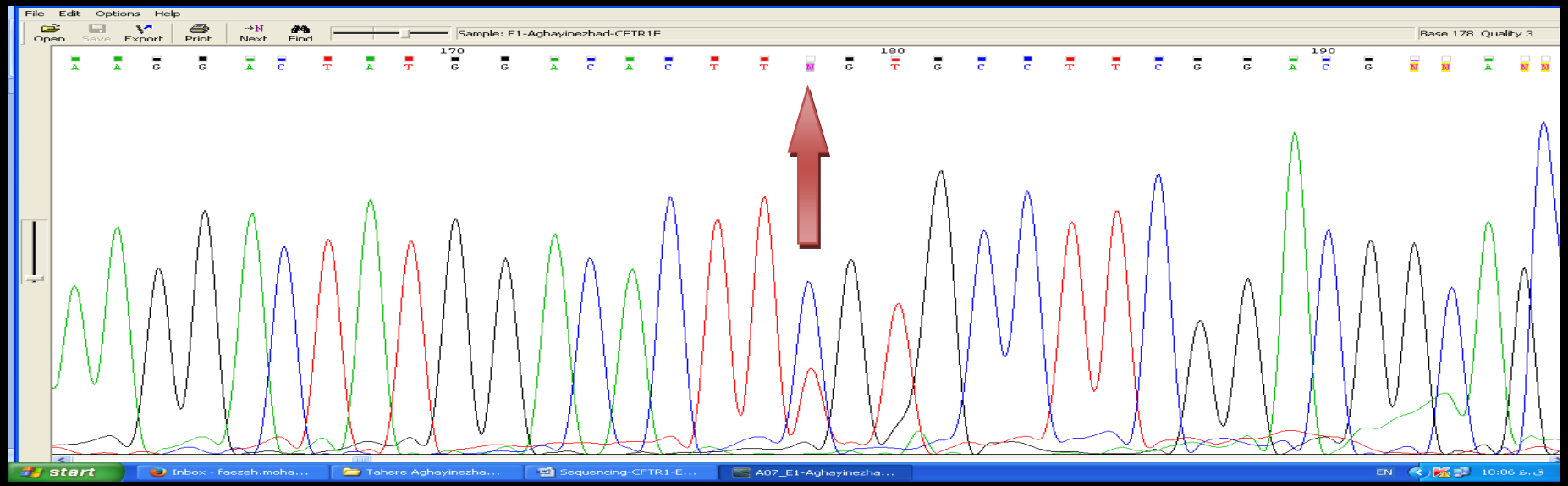
TCAAAGAATGGCACCAGTGTGAAAAAAAGCTTTTTAACCAATGACATTTGTGATATGATTATTCTAATTTAGTCTTTTT
CAGGTACAAGATATTATGAAATTACATTTTGTGTTTATGTTATTTGCAATGTTTTCTATGGAAATATTTCACAGGCAGG
AGTCCAATTTTCACTCATCTTGTTACAAGCTTAAAAGGACTATGGACACTTCGTGCCTTCGGACGGCAGCCTTACTTTG
AA

Point Mutation

T

>E1-[redacted]equence exported from A07_E1-Aghayinezhad-CFTR1F_2015-05-19.ab1
NNNNNNNNNNNNNNNNTNGTGNNNTGANTATTCTAATTTAGTCTTTTTCAGGTACAAGATATTATGAAATTACNNTTNNT
GTTTATGTTATTTGCAATGTTTTCTATGGAAATATTTCACAGGCAGGAGTCCAATTTTCACTCATCTTGTTACAAGCTT
AAAAGGACTATGGACACTTNGTGCCTTCGGACGNNANNNNTTACTTTGNAAN

Point Mutation



Embryo 2, CFTR1, Homozygous Mutation (affected)

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Preimplantation Genetic Diagnosis

Cystic Fibrosis

E2 (Mutated)

Embryos ID: E2
Mutation: c.3196C>T (R1066C)
PCR Date: 1394.02.27
Sequencing Date: 1394.02.29

Parents: [redacted]
Sampling Date: 1394.02.23
Primer Set: CFTR1
Primer Set: CFTR1F

Wild Type Sequence:

TCAAAGAATGGCACCAGTGTGAAAAAAAGCTTTTTAACCAATGACATTTGTGATATGATTATTCTAATTTAGTCTTTTT
CAGGTACAAGATATTATGAAATTACATTTTGTGTTTATGTTATTTGCAATGTTTTCTATGGAAATATTTCACAGGCAGG
AGTCCAATTTTCACTCATCTTGTTACAAGCTTAAAAGGACTATGGACACTTTGTGCCTTCGGACGGCAGCCTTACTTTG
AA

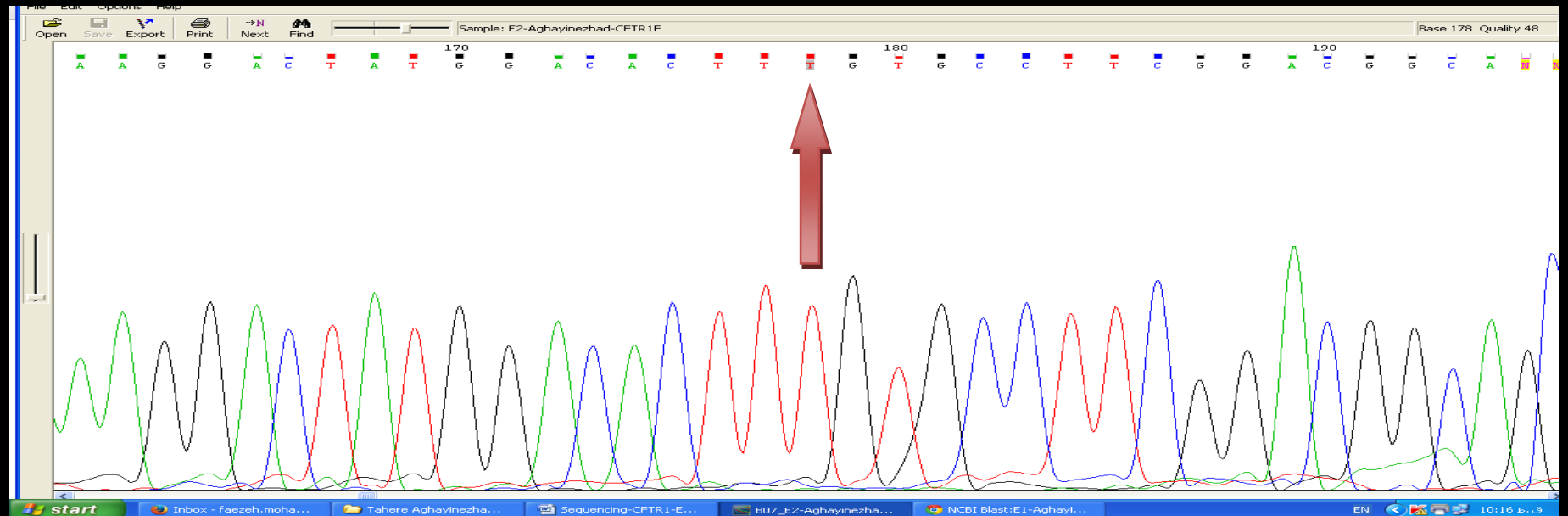
T

Point Mutation

>E2-Ag[redacted]uence exported from B07_E2-Aghayinezhad-CFTR1F_2015-05-19.ab1

NNNNNNNNNNNNNNNTTGTGNNNNGANTATTCTAATTTAGTCTTTTTCAGGTACAAGATATTATGAAATTACNTTTTGT
GTTTATGTTATTTGCAATGTTTTCTATGGAAATATTTCACAGGCAGGAGTCCAATTTTCACTCATCTTGTTACAAGCTT
AAAAGGACTATGGACACTTTGTGCCTTCGGACGGCANNNTTACTTTGAAN

Point Mutation



Embryo 2, CFTR2, Homozygous Mutation (affected)

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Preimplantation Genetic Diagnosis

Cystic Fibrosis

E2 (Mutated)

Embryos ID: E2
Mutation: c.3196C>T (R1066C)
PCR Date: 1394.02.27
Sequencing Date: 1394.03.03

Parents: Aghayinezhad-Aghayi
Sampling: [redacted]
Primer Set: CFTR2
Primer Set: CFTR2F

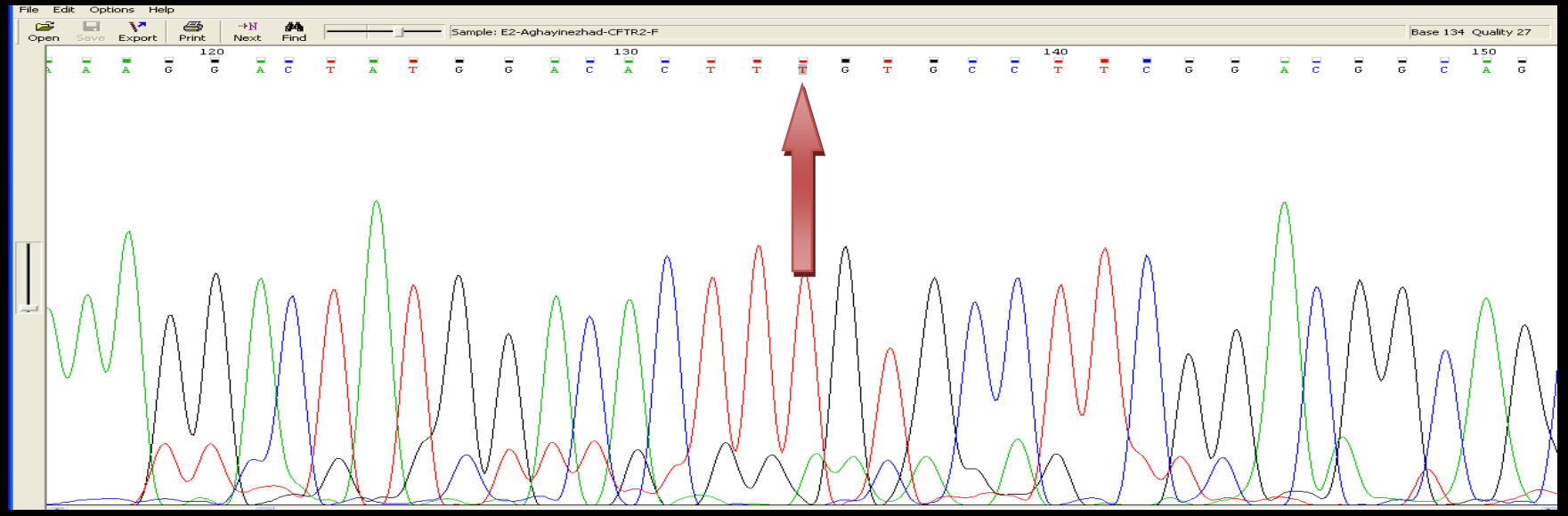
Wild Type Sequence:

AATGACATTTGTGATATGATTATTCTAATTTAGTCTTTTTCAGGTACAAGATATTATGAAATTACATTTTGTGTTTATG
TTATTTGCAATGTTTTCTATGGAAATATTTCACAGGCAGGAGTCCAATTTTCACTCATCTTGTTACAAGCTTAAAAGGA
CTATGGACACTTCGTGCCTTCGGACGGCAGCCTTACTTTGAAACTCTGTTCCACAAAGCTCTGAATTTACATACTGCCA
ACTGGTTCTTGTCCTGTCAACACTGCGCTGGTTCCAAATGAGAATAGAAATGATTTTTGTCATCTTCTTCATTGCTGT
TACCTTCATTTCCATTTTAACAACAGGTACTATGAACTCATTAACTTTAGCTAAGCATTTAAG

T Point Mutation

>E2-A[redacted]uence exported from B10_E2-Aghayinezhad-CFTR2-F_2015-05-24.ab1

NNNNNNNNNNNNTNNNNNTTACATTTTGTGTTTATGTTATTTGCNATGTTTTCTATGGAAATATTTCACAGG
CAGGAGTCCAATTTTCACTCATCTTGTTACAAGCTTAAAAGGACTATGGACACTTTGTGCCTTCGGACGGCA
GCCTTACTTTGAAACTCTGTTCCACAAAGCTCTGAATTTACATACTGCCAACTGGTTCTTGNACCTGNCAAC
ACTGCGCTGGTTCCAAATGAGAATAGAAATGATTTTTGTCATCTTCTTCANTGCTGTTACCTTCATTTCNAT
TTTAACAACAGGTACTANNNACTCNTTANCTTNNNNNNNNNNTTNAAGNAN Point Mutation



Embryo 2, CFTR4, Reverse Homozygous Mutation (affected)

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Preimplantation Genetic Diagnosis

Cystic Fibrosis

E2 (Mutated)

Embryo's ID: E2
Mutation: c.3196C>T (R1066C)
PCR Date: 1394.02.27
Sequencing Date: 1394.03.03

Parents [redacted]
Sampling Date: 1394.02.23
Primer Set: CFTR4
Primer Set: CFTR4R

Wild Type Sequence:

TCACAGGCAGGAGTCCAATTTTCACTCATCTTGTTACAAGCTTAAAAGGACTATGGACACTTCGTGCCTTCGGACGGCAGCCTTACTTTGAAACTCTGTTCCACA
AAGCTCTGAATTTACATACTGCCAACTGGTTCTTGTACCTGTCAACACTGCGCTGGTTCCAA[redacted]

T Point Mutation

Complementary Sequence:

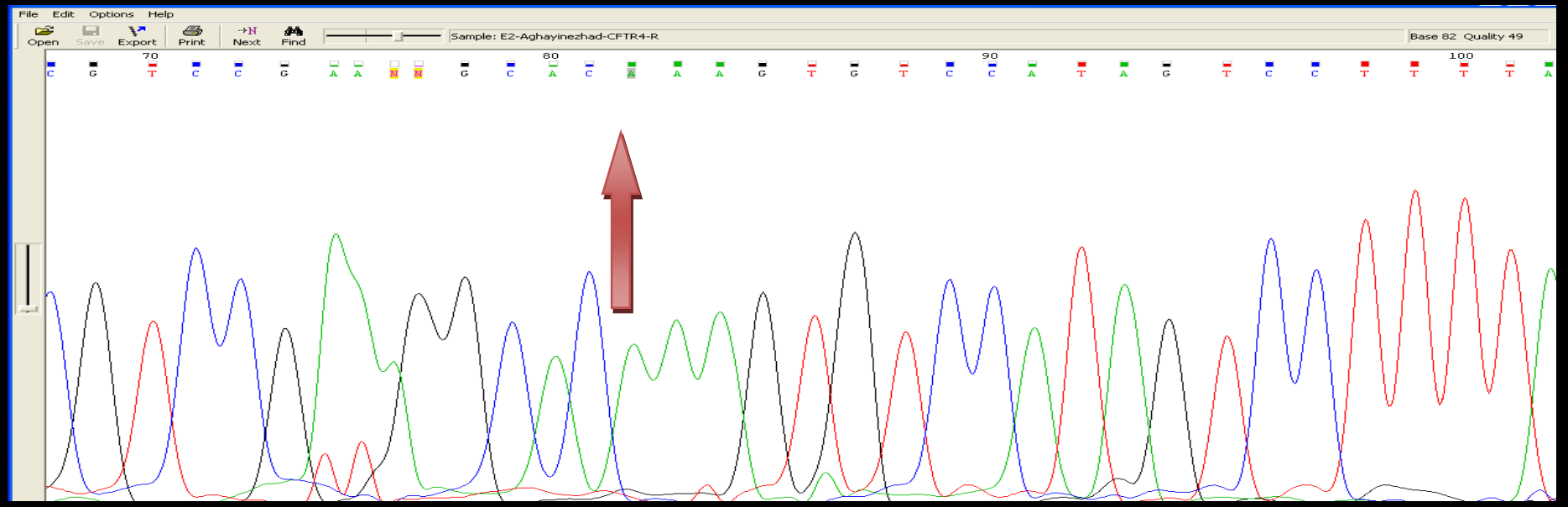
TTCTCATTTGGAACCAGCGCAGTGTTGACAGGTACAAGAACCAGTTGGCAGTATGTAAATTCAGAGCTTTGTGGAACAG
AGTTTCAAAGTAAGGCTGCCGTCCGAAGGCACGAAGTGTCCATAGTCCTTTTAAGCTTGTAACAAGATGAGTGAAAATT
GGACTCCTGCCTGTGA

Point Mutation

>E2-Ag[redacted]quence exported from D10_E2-Aghayinezhad-CFTR4-R_2015-05-24.ab1

NNNNNNNNNNGNNNGCNNNNTGNNNNNCAGNANCTTTGTGGANCAGNNNTTTCAAANGTAAGGCTGCCGTCCGAANNGC
ACAAAGTGTCCATAGTCCTTTTAAGCTNNTAACAAGANGNNNGAAAATNNGGNNNCCTGCCTGTNNN

Point Mutation



Embryo 3, CFTR1, homozygous, wild type (not affected)

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Preimplantation Genetic Diagnosis

Cystic Fibrosis

E3 (Normal)

Embryos ID: E3
Mutation: c.3196C>T (R1066C)
PCR Date: 1394.02.27
Sequencing Date: 1394.02.29

Parents: [redacted]
Sampling Date: 1394.02.23
Primer Set: CFTR1
Primer Set: CFTR1F

Wild Type Sequence:

TCAAAGAATGGCACCAGTGTGAAAAAAAGCTTTTTAACCAATGACATTTGTGATATGATTATTCTAATTTAGTCTTTTT
CAGGTACAAGATATTATGAAATTACATTTTGTGTTTATGTTATTTGCAATGTTTTCTATGGAAATATTTCACAGGCAGG
AGTCCAATTTTCACTCATCTTGTTACAAGCTTAAAAGGACTATGGACACTTCGTGCCTTCGGACGGCAGCCTTACTTTG
AA

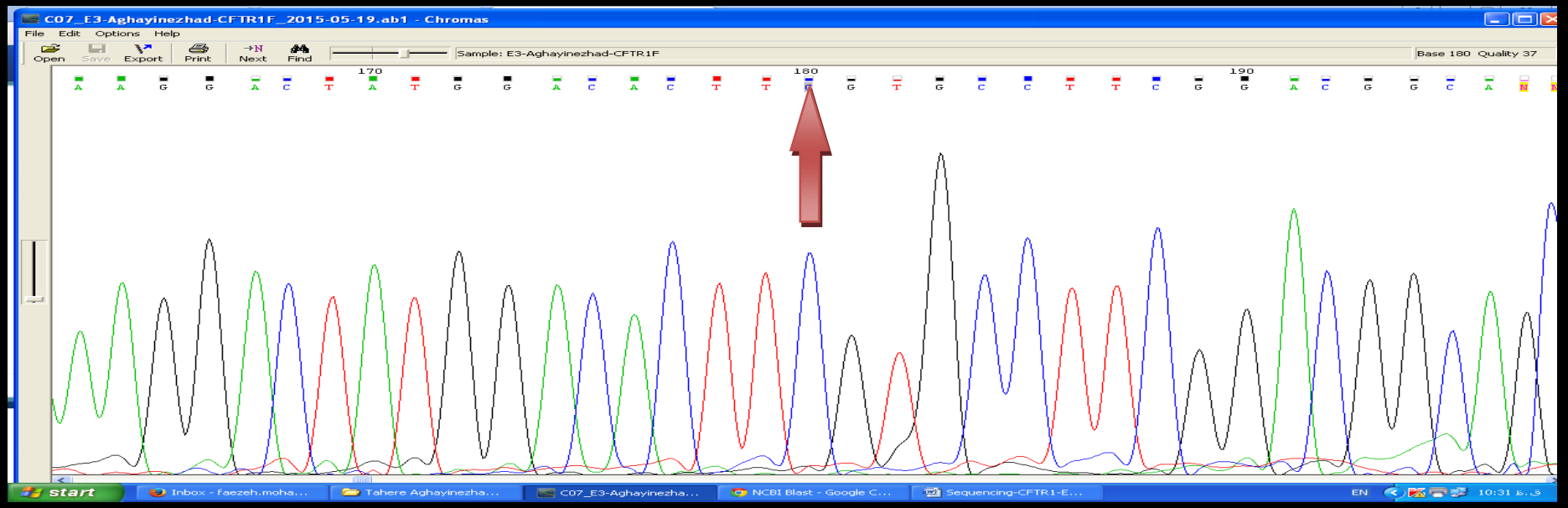
Point Mutation

T

>E3-[redacted] sequence exported from C07_E3-Aghayinezhad-CFTR1F_2015-05-19.ab1

NNNNNNNNNGTNNNNNTGNNNNNTCNAATTTNNTCNNTTTCAGNGTACAAGANATTATGAAATTACNNTTTGTGTTTAT
GTTATTTGCAATGTTTTCTATGGAAATATTTCACAGGCAGGAGTCCAATTTTCACTCATCTTGTTACAAGCTTAAAAGG
ACTATGGACACTTCGTGCCTTCGGACGGCANNNTTACTTTGAAN

Normal



Embryo 3, CFTR2, homozygous, wild type (not affected)

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا

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آزمایشگاه ژنتیک مولکولی

Preimplantation Genetic Diagnosis

Cystic Fibrosis

E3 (Normal)

Embryos ID: E3
Mutation: c.3196C>T (R1066C)
PCR Date: 1394.02.27
Sequencing Date: 1394.03.03

Parents: [redacted]
Sampling Date: 1394.02.23
Primer Set: CFTR2
Primer Set: CFTR2F

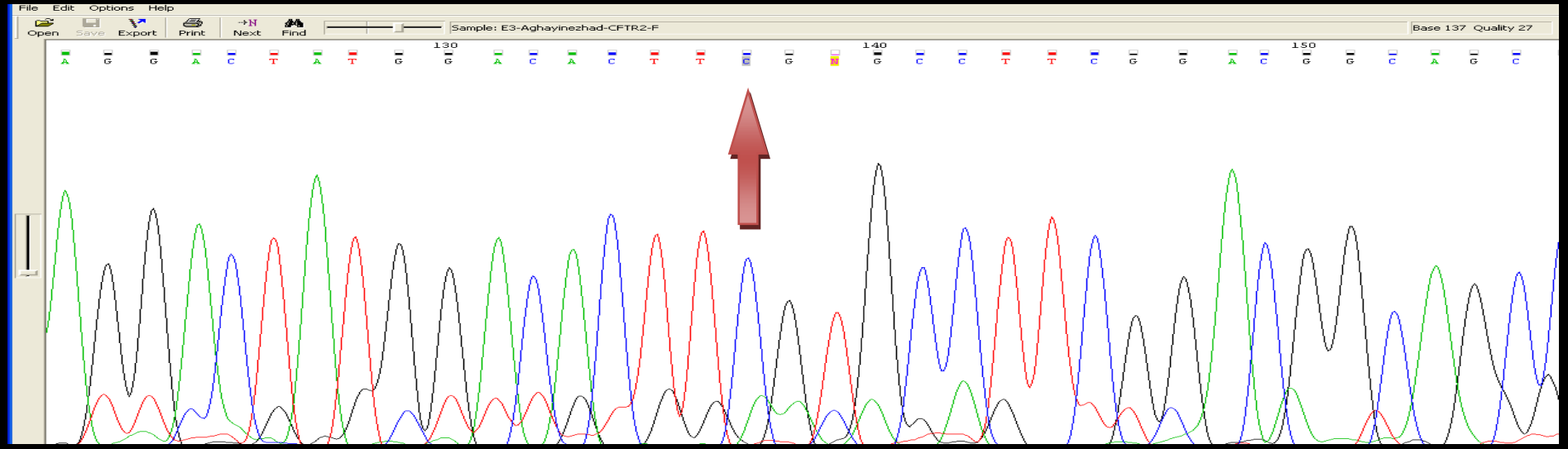
Wild Type Sequence:

AATGACATTTGTGATATGATTATTCTAATTTAGTCTTTTTCAGGTACAAGATATTATGAAATTACATTTTGTGTTTATG
TTATTTGCAATGTTTTCTATGGAAATATTTCACAGGCAGGAGTCCAATTTTCACTCATCTTGTTACAAGCTTAAAAGGA
CTATGGACACTTCGTGCCTTCGGACGGCAGCCTTACTTTGAAACTCTGTTCCACAAAGCTCTGAATTTACATACTGCCA
ACTGGTTCTTGTCCTGTCAACACTGCGCTGGTTCCAAATGAGAATAGAAATGATTTTTGTCATCTTCTTCATTGCTGT
TACCTTCATTTCCATTTTAACAACAGGTACTATGAACTCATTAACTTTAGCTAAGCATTTAAG

T — Point Mutation

>E3-A[redacted] sequence exported from F10_E3-Aghayinezhad-CFTR2-F_2015-05-24.ab1

NNNNNNNNNNNNNTANNNNNNTACNTTTTGTGTTNATGTTATTTGCAATGTTTTCTATGGAANNNTTTCACA
GGCAGGAGTCCAATTTTCACTCATCTTGTTACAAGCTTAAAAGGACTATGGACACTTCGNGCCTTCGGACGG
CAGCCTTACTTTGAAACTCTGTTCCACAAAGCTCTGAATTTACATACTGCCAACTGGTCTTGNACCTGTCA
ACACTGCNCTGGTTCCAAATGAGAATAGAAATGATTTTTGTCATCTTCTTCATTGCTGTTACCTTCATTTCC
ATTTTAACAACAGGTACTATGAACTCNTTAACTTTANNNANNNNTTTAAGA — Normal



Embryo 3, CFTR4, Reverse homozygous, wild type (not affected)

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا

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Preimplantation Genetic Diagnosis

Cystic Fibrosis

E3 (Normal)

Embryo's ID: E3
Mutation: c.3196C>T (R1066C)
PCR Date: 1394.02.27
Sequencing Date: 1394.03.03

Parents: [redacted]
Sampling Date: 1394.02.23
Primer Set: CFTR4
Primer Set: CFTR4R

Wild Type Sequence:

TCACAGGCAGGAGTCCAATTTTCACTCATCTTGTTACAAGCTTAAAAGGACTATGGACACTTCGTGCCTTCGGACGGCAGCCTTACTTTGAAACTCTGTTCCACA
AAGCTCTGAATTTACATACTGCCAACTGGTTCTTGTACCTGTCAACACTGCGCTGGTTCCAA[redacted]

T Point Mutation

Complementary Sequence:

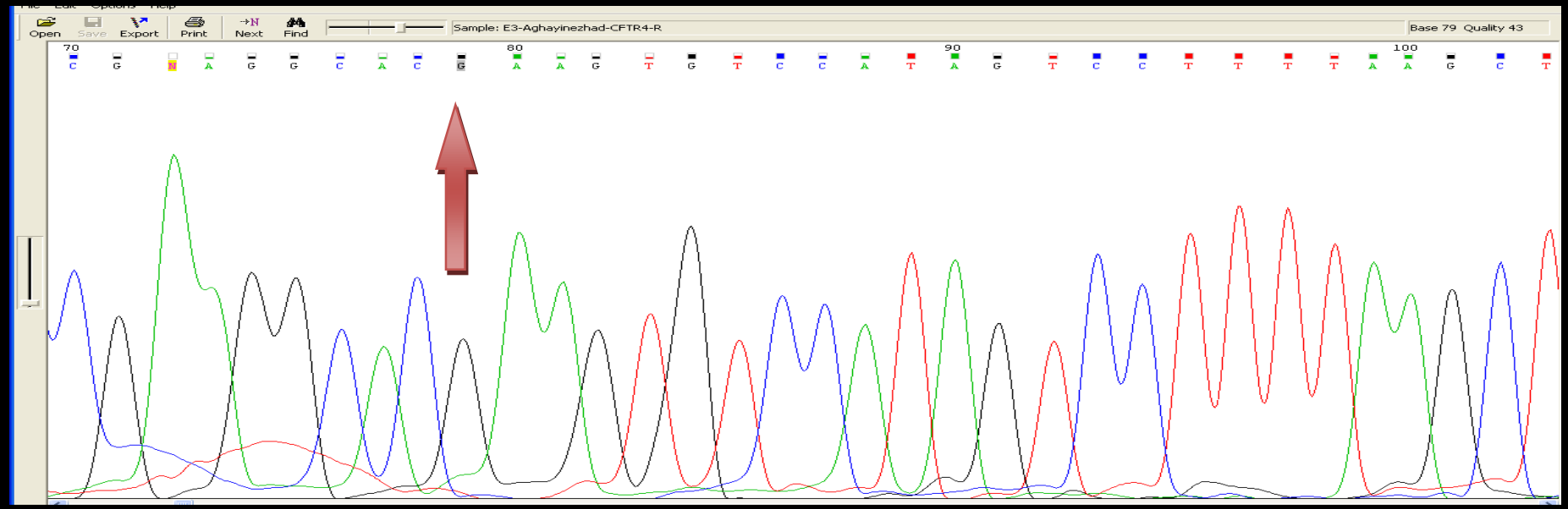
TTCTCATTTGGAACCAGCGCAGTGTTGACAGGTACAAGAACCAGTTGGCAGTATGTAAATTCAGAGCTTTGTGGAACAG
AGTTTCAAAGTAAGGCTGCCGTCCGAAGGCACGAAGTGTCCATAGTCCTTTTAAGCTTGTAACAAGATGAGTGAAAATT
GGACTCCTGCCTGTGA

Point Mutation

>E3-[redacted]equence exported from E10_E3-Aghayinezhad-CFTR4-R_2015-05-24.ab1

NNNNNNNNNNNNNNNNCNNNNTGNNNNCAGAANCTTTGTGGACAGANNTTTCAAAGTAAGGCTGCCGTCCGNAGGCACG
AAGTGTCCATAGTCCTTTTAAGCTTGTAACAAGATGAGTGAAAATTGNACNNCTGCCTGNNNN[redacted]N
C

Normal



Sex determination of unaffected embryos
E1: SRY positive
E3: SRY negative

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Preimplantation Genetic Diagnosis

Cystic Fibrosis

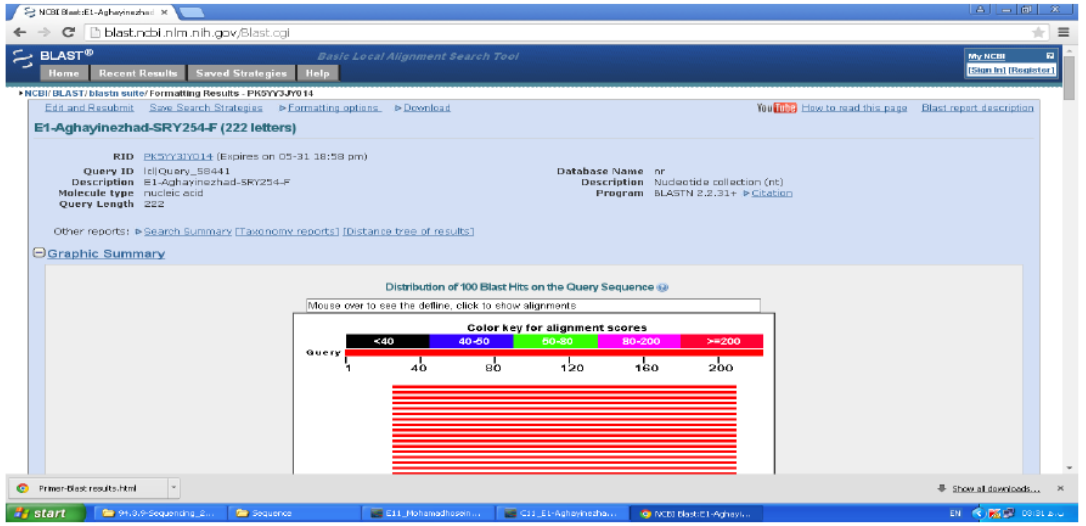
SRY

E1 (Male)

Embryos ID: E1
Sampling Date: 1394.02.23
PCR Date: 1394.02.24
Sequencing Date: 1394.03.09

Parents: [redacted]

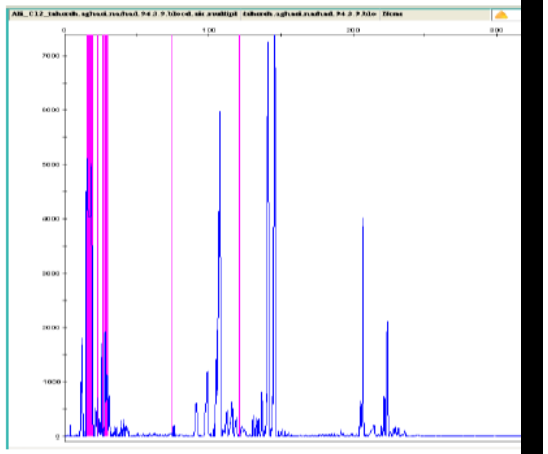
Primer Set: SRY-254
Primer Set: SRY-254F



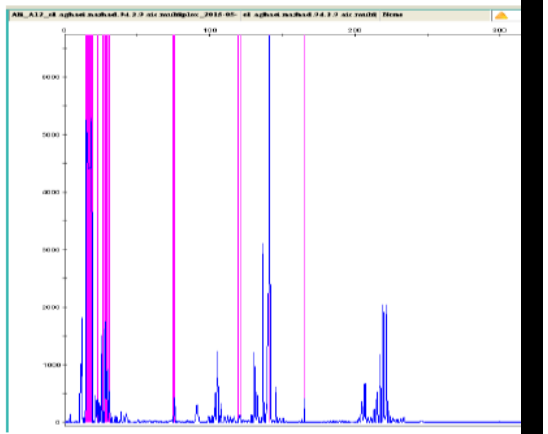
E1

Rule out of contamination

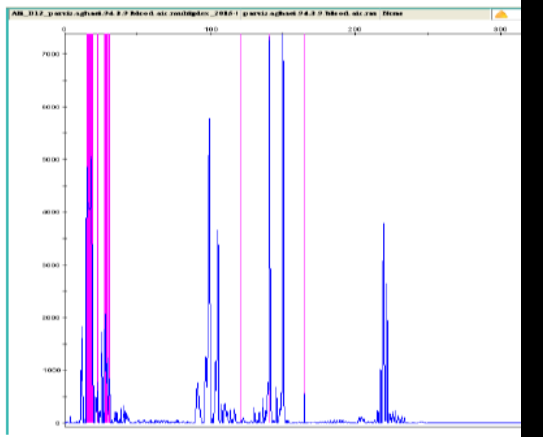
Mother



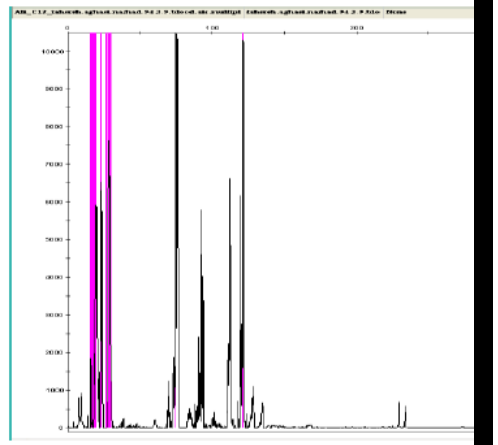
E1



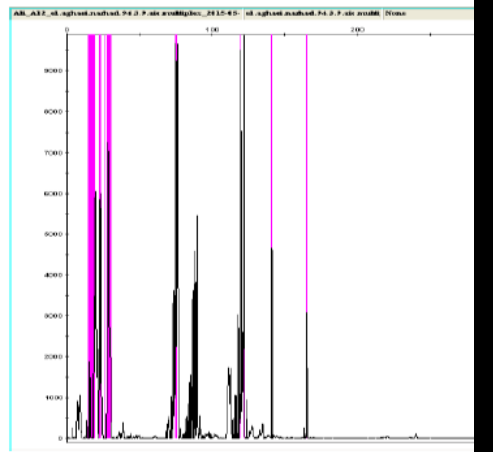
Father



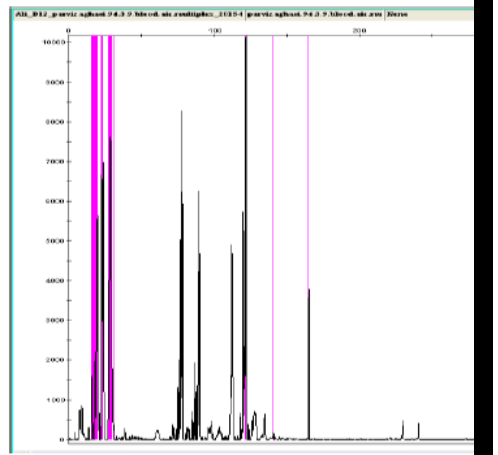
Mother



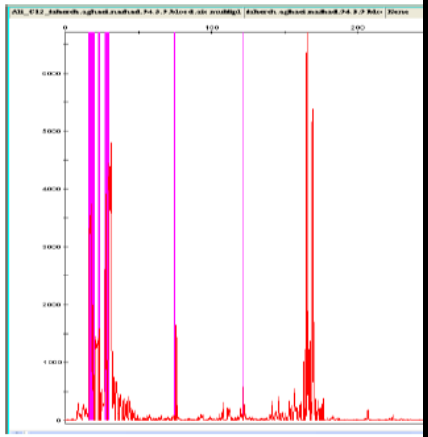
E1



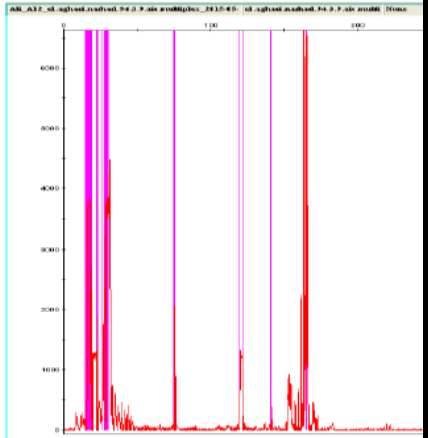
Father



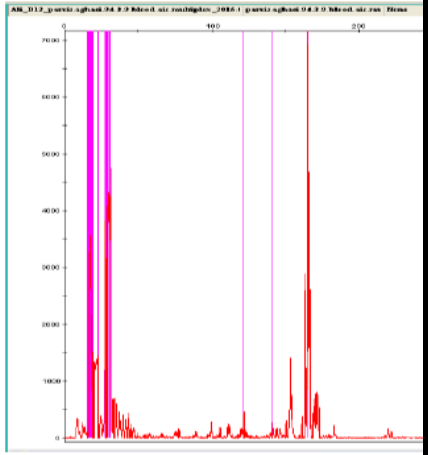
Mother



E1



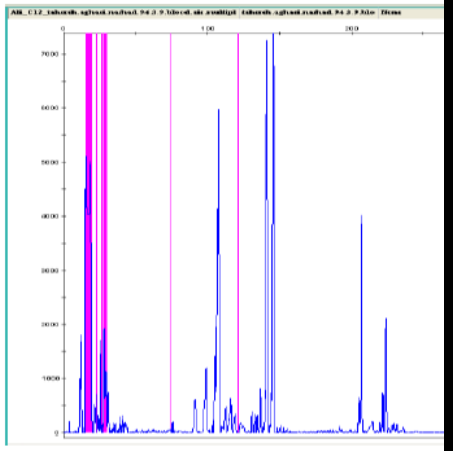
Father



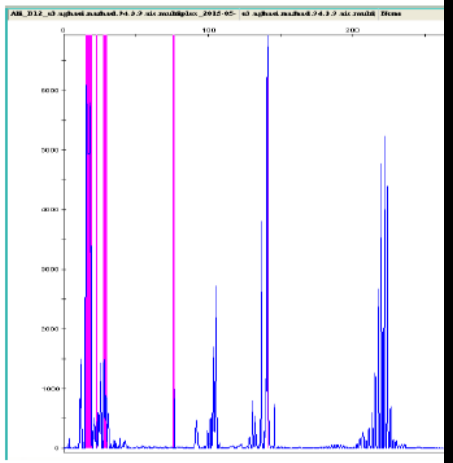
E3

Rule out of contamination

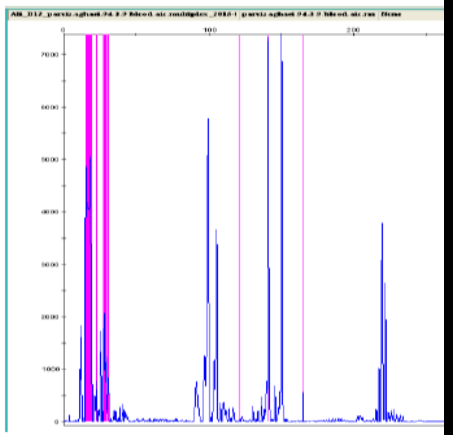
Mother



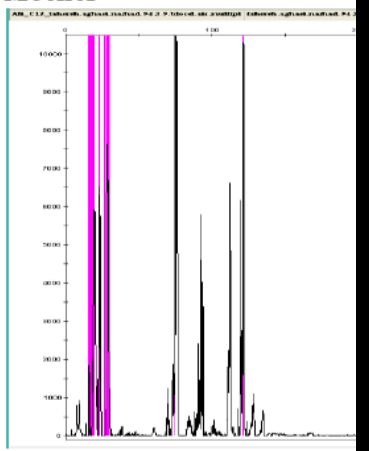
E3



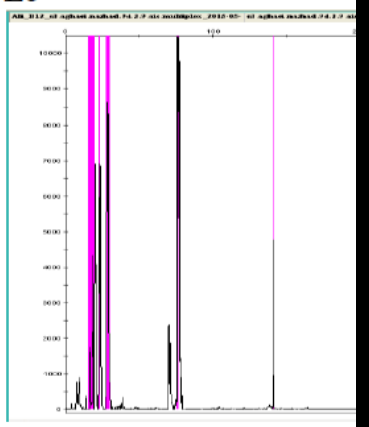
Father



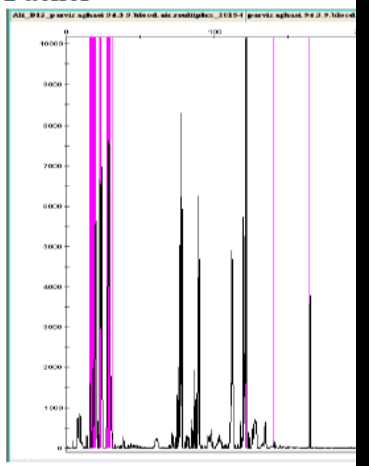
Mother



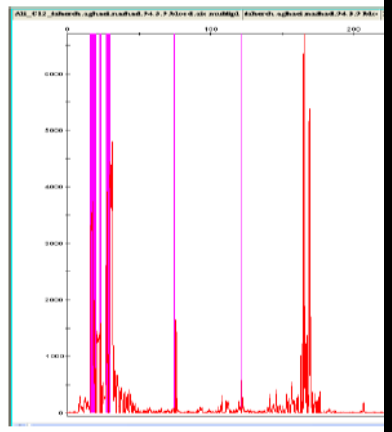
E3



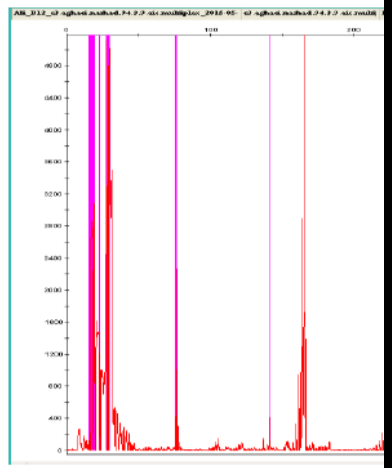
Father



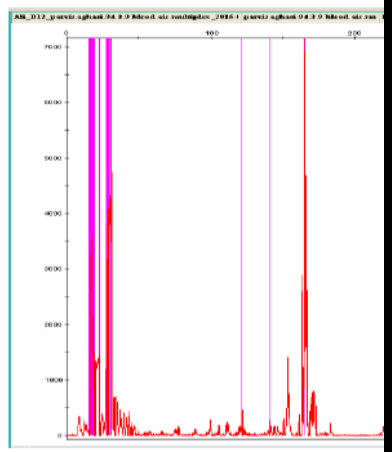
Mother



E3



Father



Summary of results

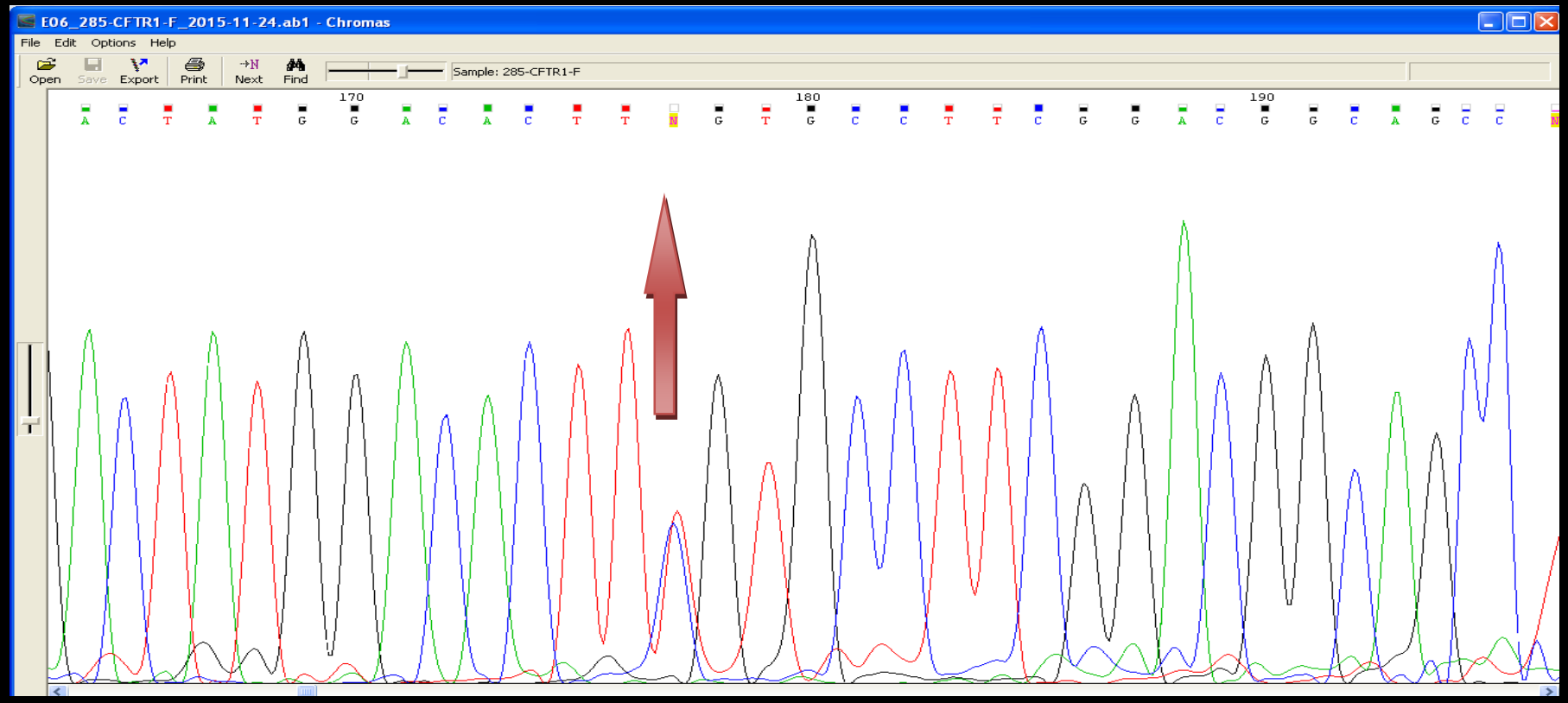
ID	CFTR1	CFTR2	CFTR3	CFTR4	SRY	Final Result
E1	Normal Heterozygous	Normal Heterozygous	Normal Heterozygous	Normal Heterozygous	+	قابل انتقال
E2	Mutated Homozygous	Mutated Homozygous	Mutated Homozygous	Mutated Homozygous	-	غيرقابل انتقال
E3	Normal	Normal	Normal	Normal	-	قابل انتقال
E4	No Result	No Result	No Result	No Result	-	غيرقابل انتقال

Embryo Transfer

- Tow unaffected embryos (E1 and E3) were transferred (Shahrivar 1394, Sep 2015)
- The mother got pregnant (singleton pregnancy) and prenatal diagnosis was carried out on Aban 1394, Oct 2015

PND

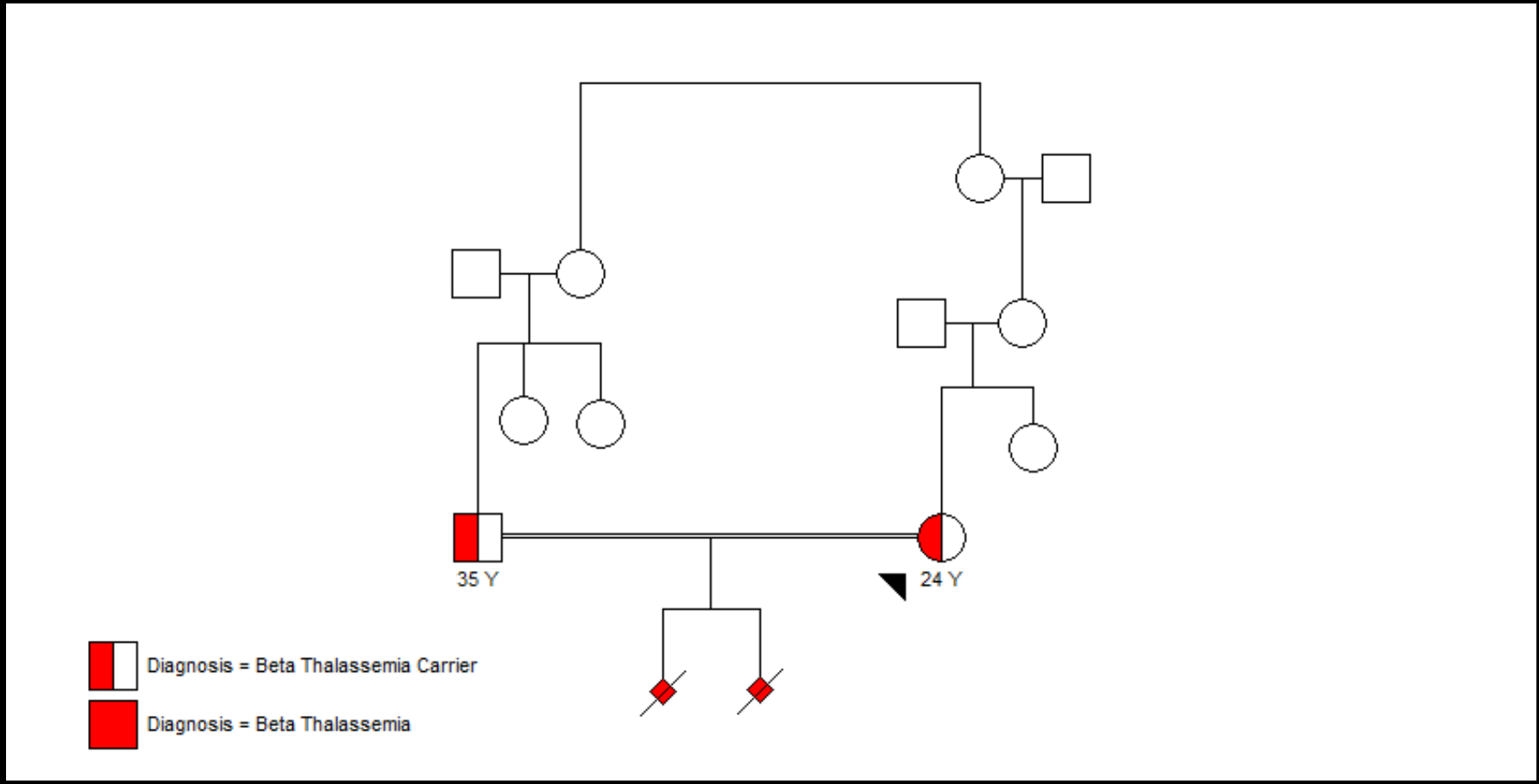
- Fetus was unaffected (carrier)



Birth of healthy newborn

- Healthy baby was born (27 Ordibehesht 1395, 16 May 2016)

Third family



Previous investigations

Methods:

1. ARMS PCR amplification method.
2. PCR/RFLP for informative RFLP markers in the *Beta-globin* gene region.

Molecular results are as follows:

Patient's Name	Beta Nucleotide changes	Effect	Phenotype	Informative RFLP	Phenotype	MCV	MCH	A2
[redacted]	IVSI-6	Pathogenic	Carrier(ناقل)	*Hind*IIIG-*Hind*IIIA	Carrier	64.6	20.5	3.6
	IVSI-6	Pathogenic	Carrier(ناقل)	*Hind*IIIG-*Hind*IIIA	Carrier	64.8	20.8	3.8
	IVSI-6	Pathogenic	Affected(مبتلا)	*Hind*IIIG-*Hind*IIIA	Affected	-	-	-

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کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Preimplantation Genetic Diagnosis

Beta-thalassemia

Patient Name: [redacted]
Partner [redacted]
Mutation: IVSI-6
Sampling Date: 1394.03.20
PCR Date: 1394.03.26
Primer Set: HBB3
Sequencing Date: 1394.04.01
Primer Set: HBB3F

Wild Type Sequence:

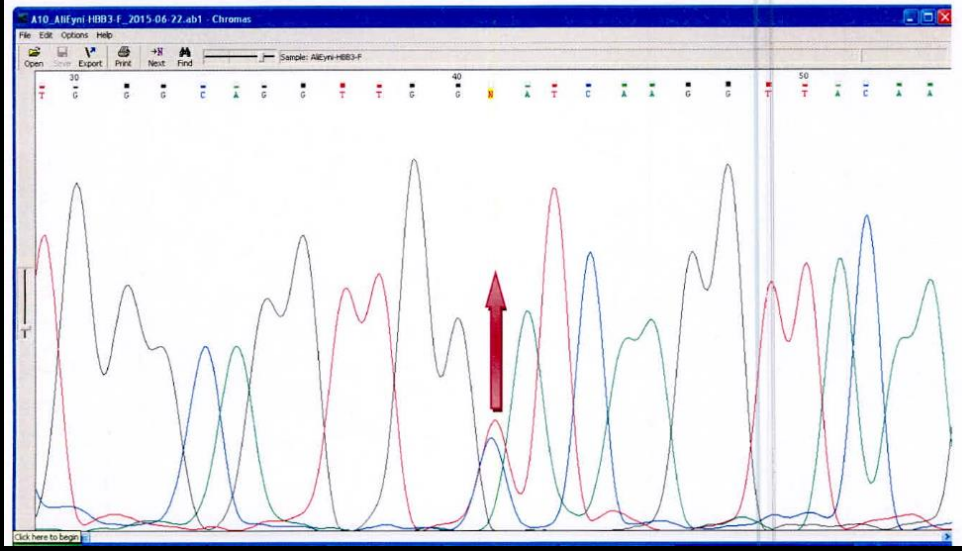
Point Mutation

GAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCAA
GGTTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGCAC
TGACTCTCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCT GGACCCAGAGGTTCTTTGAGT
CCTTTGGGGATCTGTCCACTCCTGA

>AliEyni-HBB3-F sequence exported from A10_AliEyni-HBB3-F_2015-06-22.ab1

Point Mutation

NNNNNNNNNNNNNNNNGTGGTGANGCNCTGGGCAGGTTGGNATCAAGGTTACAAGACAGGTTTAAGGAGACCA
ATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGCACTGACTCTCTCTGCCTATTGG
TCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGANCN
NNCCCNCTCCTGNNN



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آزمایشگاه ژنتیک مولکولی

Preimplantation Genetic Diagnosis

Beta-thalassemia

Patient Name: [redacted]
Partner: [redacted]
Mutation: IVSI-6 T>C
Sampling Date: 1394.03.20
PCR Date: 1394.03.26
Primer Set: HBB3
Sequencing Date: 1394.04.06
Primer Set: HBB3R

Wild Type Sequence:

Point Mutation

AAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCAA
GGTTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGCAC
TGACTCTCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGT
CTTTGGGGATCTGTCCACTCCTGA

Reverse Complement:

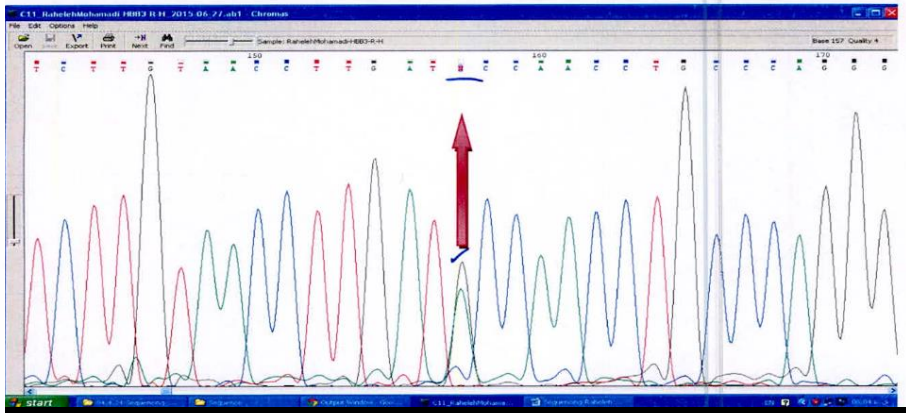
TCAGGAGTGGACAGATCCCCAAAGGACTCAAAGAACCTCTGGGTCCAAGGGTAGACCACCAGCAGCCTAAGGG
TGGGAAAATAGACCAATAGGCAGAGAGAGTCAGTGCCTATCAGAAACCCAAGAGTCTTCTCTGTCTCCACATG
CCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAACCTTGATACCAACCTGCCCAGGGCCTCACCACCAAC
TTCATCCACGTTCACCTTGCCCCACAGGGCAGTAACGGCAGACTTC

Point Mutation

>RahelehMohamadi-HBB3-R-H sequence exported from C11_RahelehMohamadi-HBB3-R-H_2015-06-27.ab1

NNNNNGNNNNGNNANNNCACCAGCAGCCTAAGGGTGGNNNNNAGACCAATAGGCAGANAGAGTCAGTGCCTATCANAAA
CCCAAGAGTCTTCTCTGTCTCCACATGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAACCTTGATNCCAACCTG
CCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTTGCCCCACAGGGCANNNNNNNNCAGACNNNNN

Point Mutation



Biopsy checklist

Whole Genome Amplification Method:

Laboratory Checklist

Father's name: **Family ID:**

Mother's name: [redacted] **Date:** 94.12.16

❖ ***Embryo biopsy***

Date and time: 94.12.16

Done by: Dr. Sadeghi

checked by: Kiani-Rezvani-Abolhathi

No	Subject	Embryo ID				
		E-1	E-2	E-3	E-4	E-5
1	Transfering the embryo to the labeled dish	2cell 12A	2cell 12A	2cell 12A	2cell 12AB	2cell 12B
2	Transferring the blastomeres to the labeled microtube	8:05	8:07	8:09	8:11	8:16

No	Subject	Embryo ID				
		E-6	E-7	E-8	E-9	E-10
1	Transfering the embryo to the labeled dish	2cell 10B	2cell 8AB	2cell 12A	2cell 12B	2cell 10B
2	Transferring the blastomeres to the labeled microtube	8:18	8:20	8:21	8:23	8:25

Signed:

Embryologist Dr Sadeghi

Geneticist Dr Ghaffari

Checker

Freezing checklist

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Family ID: راحله محمدی - سید علی عینی

Father's name: Ali Eini **Family ID:**

Mother's name: [redacted] **Date:** 94.12.17

❖ ***Embryo Frozen*** Date and time: 94.12.17

Done by: Fathi checked by: Rezvani

در بیوپسی روز ۳ به ما توی نداریم بخاطر کیفیت بد جنین

ولی فریز نشده است

No	Subject	Embryo ID				
		E-1	E-2	E-3	E-4	E-5
1	Transfering the embryo to the labeled dish	✓ 11:40	✓ 11:44	✓ 11:50	✓ 11:54	✓ 12:02
2	Transferring the embryo to the labeled cryotop	✓ 11:48	✓ 11:52	✓ 11:58	✓ 12:07	✓ 12:10

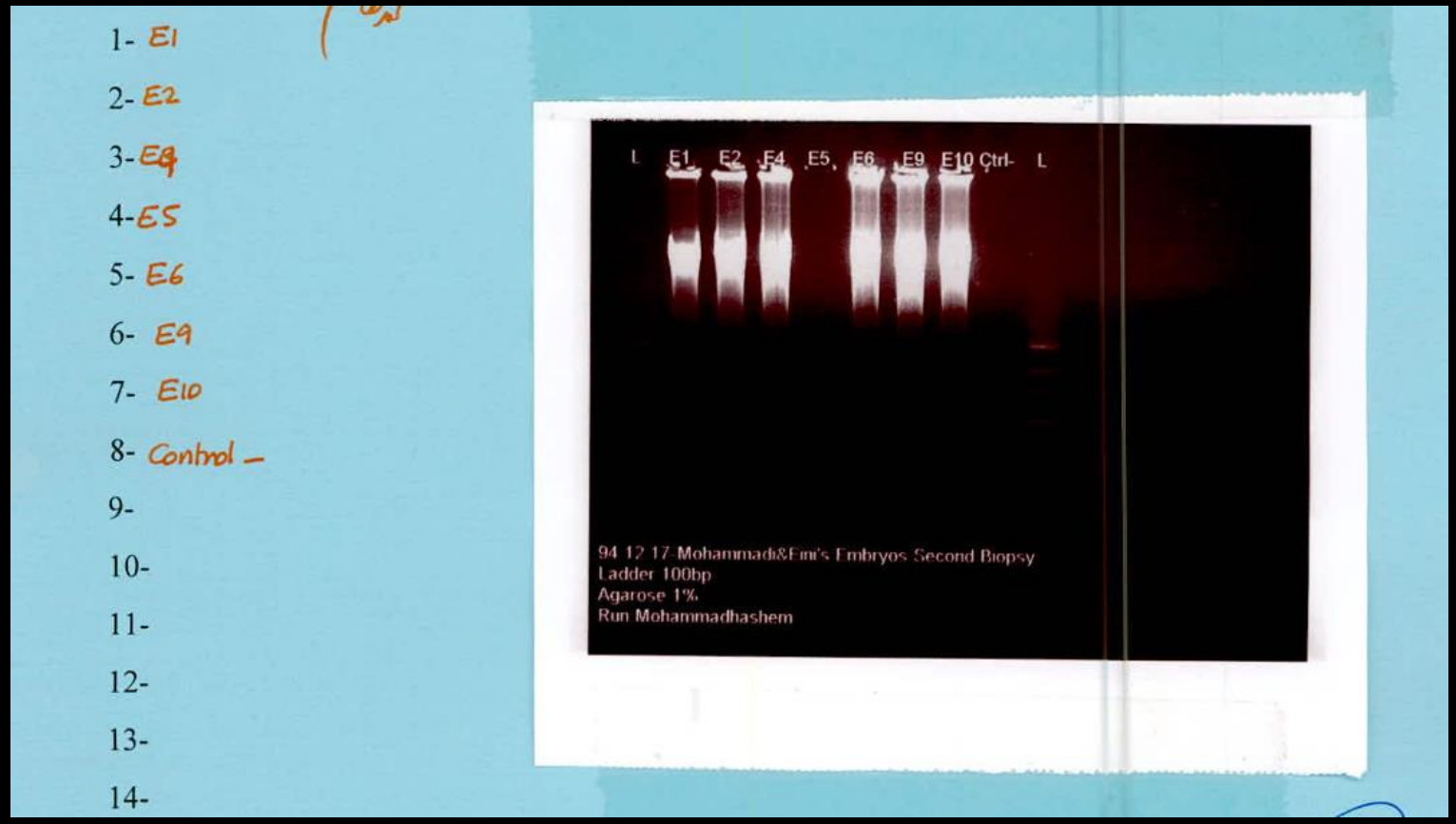
No	Subject	Embryo ID				
		E-6	E-7	E-8	E-9	E-10
1	Transfering the embryo to the labeled dish	✓ 12:13	✓ 12:15	✓ 12:26	✓ 12:28	✓ 12:42
2	Transferring the embryo to the labeled cryotop	✓ 12:20	✓ 12:24	✓ 12:39	✓ 12:36	✓ 12:50

Signed:

Done by: فتحی 94,12,17

Checked by: رضوانی 94,12,17

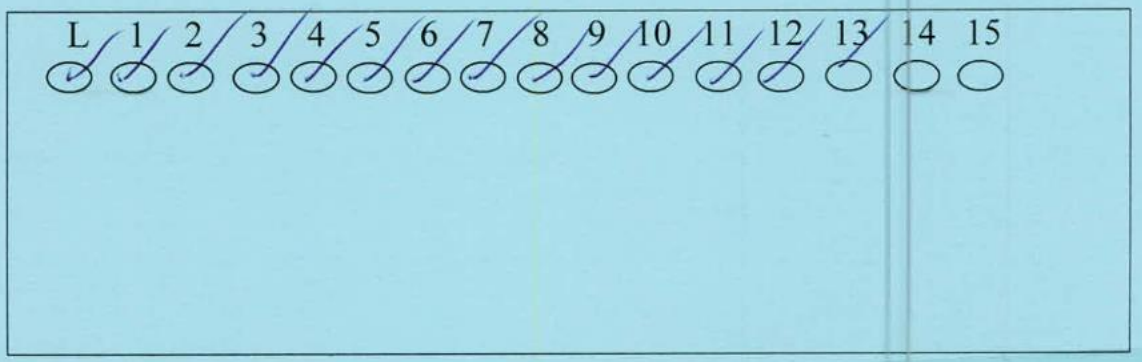
Single cell WGA



First PCR

Gel electrophoresis

Date: ۹۴/۱۲/۲۰ Test: HBB3



L: ladder

1- E۱

2- E۲

3- [illegible]

4- E ۴

5- E ۶

6- [illegible]

7- E ۷

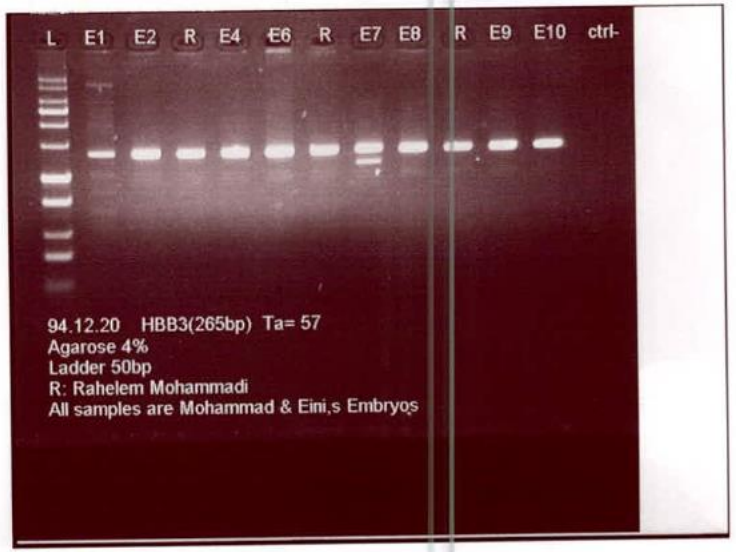
8- E ۸

9- [illegible]

10- E ۹

11- E ۱۰

12- Ctrl-



Second PCR


L: ladder
1- E1
2- E2
3-
4- E4
5- E6
6-
7- E7
8- E8
9-
10- E9
11- E10
12-
13- Ctrl-
14
L E1 E2 R E4 E6 R E7 E8 R E9 E10 R ctrl-
94.12.20 HBB N5(245bp)
Agarose 4%
Ladder 50bb
R: Raheleh Mohammadi
All samles are Mohammadi & Eini's Embryos

E1, Wild type homozygousx

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Preimplantation Genetic Diagnosis

Beta-Thalassemia

E1 (Normal)

Embryo's ID: E1
Parents' Mutation: IVSI-6 T>C (c.92+6T>C)
PCR Date: 1394.12.20
Sequencing Date: 1394.12.27

Sampling Date: 1394.12.16
Primer Set: HBB3
Primer Set: HBB3R

Wild Type Sequence:

Point mutation

GAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCA
AGGTTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGC
ACTGACTCTCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTG
AGTCCTTTGGGGATCTGTCCACTCCTGA

Reverse Complement:

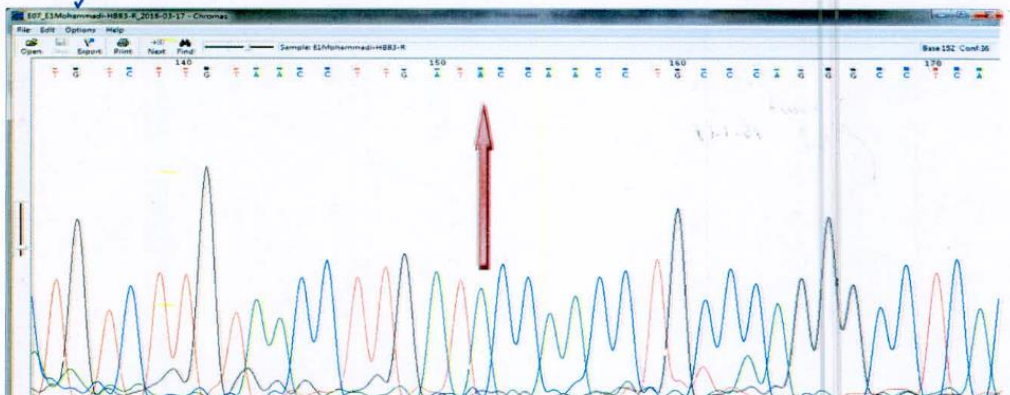
TCAGGAGTGGACAGATCCCCAAAGGACTCAAAGAACCTCTGGGTCCAAGGGTAGACCACCAGCAGCCTAAGGGTGGGAA
AATAGACCAATAGGCAGAGAGAGTCAGTGCCTATCAGAAACCCAAGAGTCTTCTCTGTCTCCACATGCCCAGTTTCTAT
TGGTCTCCTTAAACCTGTCTTGTAACCTTGATACCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTT
GCCCCACAGGGCAGTAACGGCAGACTTC

Point Mutation

>E1Mohammadi-HBB3-R sequence exported from E07_E1Mohammadi-HBB3-R_2016-03-17.ab1

NNNNNNNNNNNNNNNNNNNNNCNNGCNGCCTAGGGTGGNAANNANACCANTAGGCAGANAGAGTCANTGCCT
ATCNNNNNCCCANGAGTCTTNTCNGNCTCCACATGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAA
CCTTGATACCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTTGCCCCACAGGGCAGNNNN
NNCAGAC

Normal



E2, Heterozygous mutation

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Heterozygous Mutation

Preimplantation Genetic Diagnosis

Beta-Thalassemia

E2 (Heterozygous)

Embryo's ID: E2
Parents' Mutation: IVSI-6 T>C (c.92+6T>C)
PCR Date: 1394.12.20
Sequencing Date: 1394.12.27

[redacted]
Sampling Date: 1394.12.16
Primer Set: HBB3
Primer Set: HBB3R

Wild Type Sequence:

Point mutation

GAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCA
AGGTTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGC
ACTGACTCTCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTG
AGTCCTTTGGGGATCTGTCCACTCCTGA

Reverse Complement:

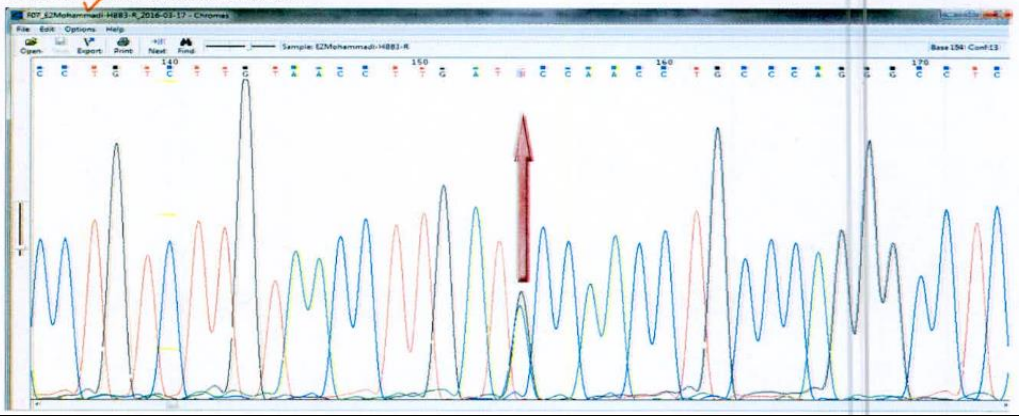
TCAGGAGTGGACAGATCCCCAAAGGACTCAAAGAACCTCTGGGTCCAAGGGTAGACCACCAGCAGCCTAAGGGTGGGAA
AATAGACCAATAGGCAGAGAGAGTCAGTGCCTATCAGAAACCCAAGAGTCTTCTCTGTCTCCACATGCCCAGTTTCTAT
TGGTCTCCTTAAACCTGTCTTGTAACCTTGATACCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTT
GCCCCACAGGGCAGTAACGGCAGACTTC

Point Mutation

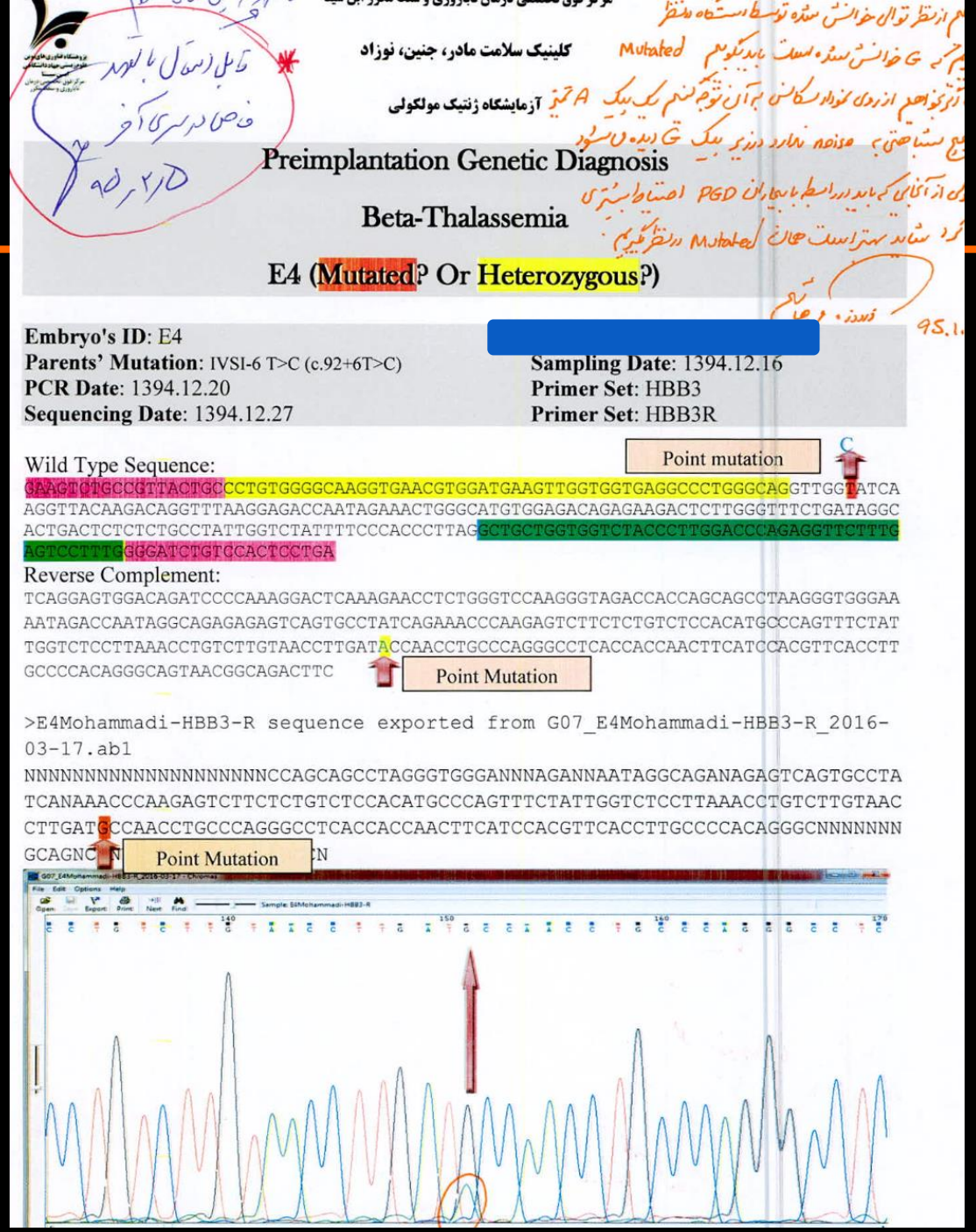
>E2Mohammadi-HBB3-R sequence exported from F07_E2Mohammadi-HBB3-R_2016-03-17.ab1

NNNNNNNNNCACCAGCAGCCTANGGTGGGANNTAGACCAATAGGCAGANAGAGTCAGTGCCTATCANAAACC
CAAGAGTCTTCTCTGTCTCCACATGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAACCTTGATNCC
AACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTTGCCCCACAGG NN
NNNNNNTAGNGANNNNNNNNN

Point Mutation



E4, Heterozygous mutation



کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Preimplantation Genetic Diagnosis

Beta-Thalassemia

E4 (Mutated? Or Heterozygous?)

Embryo's ID: E4
Parents' Mutation: IVSI-6 T>C (c.92+6T>C)
PCR Date: 1394.12.20
Sequencing Date: 1394.12.27
Sampling Date: 1394.12.16
Primer Set: HBB3
Primer Set: HBB3R

Point mutation

Wild Type Sequence:

GAAGTGTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCA
AGGTTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGC
ACTGACTCTCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTG
AGTCCTTTGGGGATCTGTCCACTCCTGA

Reverse Complement:

TCAGGAGTGGACAGATCCCCAAAGGACTCAAAGAACCTCTGGGTCCAAGGGTAGACCACCAGCAGCCTAAGGGTGGGAA
AATAGACCAATAGGCAGAGAGAGTCAGTGCCTATCAGAAACCCAAGAGTCTTCTCTGTCTCCACATGCCCAGTTTCTAT
TGGTCTCCTTAAACCTGTCTTGTAACCTTGATACCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTT
GCCCCACAGGGCAGTAACGGCAGACTTC

Point Mutation

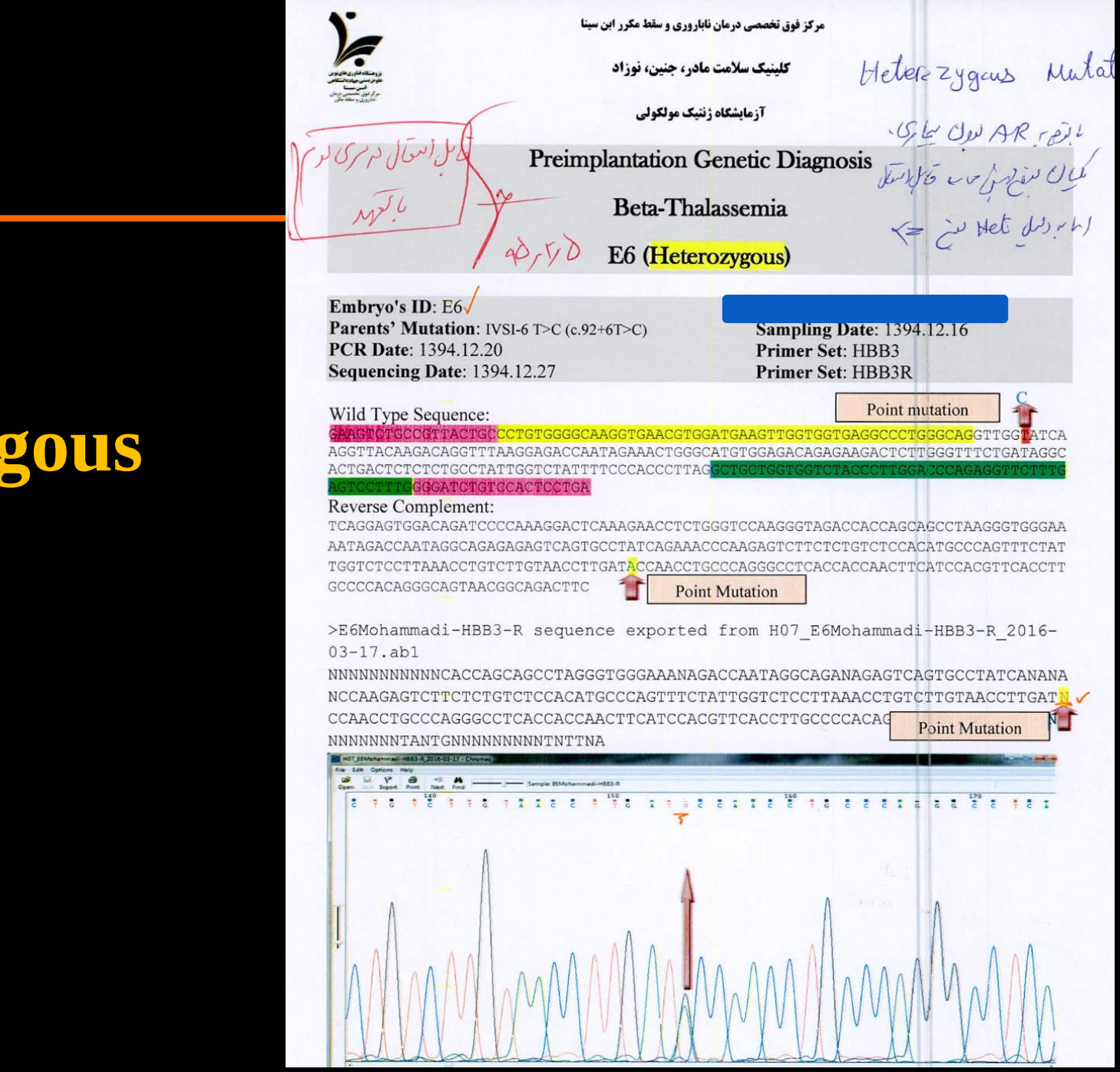
>E4Mohammadi-HBB3-R sequence exported from G07_E4Mohammadi-HBB3-R_2016-03-17.ab1

NNNNNNNNNNNNNNNNNNNNCCAGCAGCCTAGGGTGGGANNNAGANNAATAGGCAGANAGAGTCAGTGCCTA
TCANAAACCCAAGAGTCTTCTCTGTCTCCACATGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAAC
CTTGATGCCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTTGCCCCACAGGGCNNNNNNN
GCAGNC N

Point Mutation

CN

E6, Heterozygous mutation



مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Heterozygous Mutat

Preimplantation Genetic Diagnosis

Beta-Thalassemia

E6 (Heterozygous)

Embryo's ID: E6
Parents' Mutation: IVSI-6 T>C (c.92+6T>C)
PCR Date: 1394.12.20
Sequencing Date: 1394.12.27
Sampling Date: 1394.12.16
Primer Set: HBB3
Primer Set: HBB3R

Point mutation

Wild Type Sequence:

GAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCA
AGGTTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGC
ACTGACTCTCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTG
AGTCCTTTGGGGATCTGTCCACTCCTGA

Reverse Complement:

TCAGGAGTGGACAGATCCCCAAAGGACTCAAAGAACCTCTGGGTCCAAGGGTAGACCACCAGCAGCCTAAGGGTGGGAA
AATAGACCAATAGGCAGAGAGAGTCAGTGCCTATCAGAAACCCAAGAGTCTTCTCTGTCTCCACATGCCCAGTTTCTAT
TGGTCTCCTTAAACCTGTCTTGTAACCTTGATACCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTT
GCCCCACAGGGCAGTAACGGCAGACTTC

Point Mutation

>E6Mohammadi-HBB3-R sequence exported from H07_E6Mohammadi-HBB3-R_2016-03-17.ab1

NNNNNNNNNNNCACCAGCAGCCTAGGGTGGGAAANAGACCAATAGGCAGANAGAGTCAGTGCCTATCANANA
NCCAAGAGTCTTCTCTGTCTCCACATGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAACCTTGATN
CCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTTGCCCCACAG
NNNNNNNTANTGNNNNNNNNNTNTTNA

Point Mutation

E7, Wild type, homozygous

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آزمایشگاه ژنتیک مولکولی

No mutation

سری اول انتقال

Preimplantation Genetic Diagnosis

Beta-Thalassemia

✓E7 (Normal)

OK ← از نظر کاشن

از نظر STR ← قابل انتقال

با تشخیص

Embryo's ID: E7✓
Parents' Mutation: IVSI-6 T>C (c.92+6T>C)
PCR Date: 1394.12.20
Sequencing Date: 1394.12.22

Sampling Date: 1394.12.16
Primer Set: HBB3
Primer Set: HBB3R

Wild Type Sequence:

Point mutation

GAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCA
AGGTTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGC
ACTGACTCTCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTG
AGTCCTTTGGGGATCTGTCCACTCCTGA

Reverse Complement:

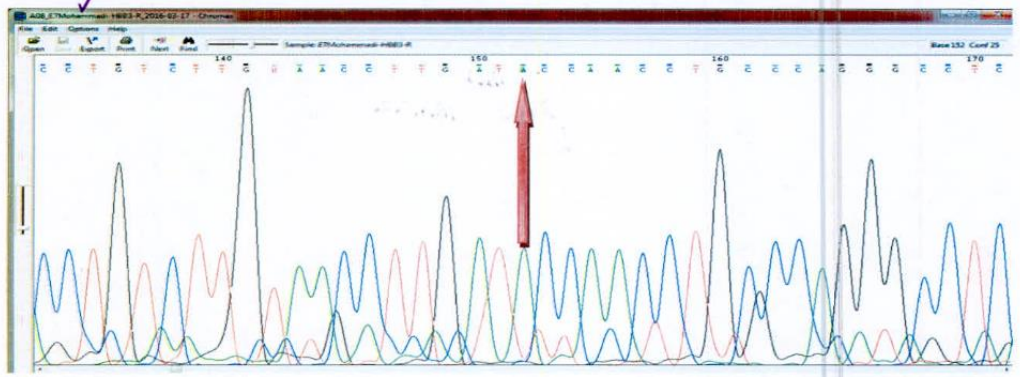
TCAGGAGTGGACAGATCCCCAAAGGACTCAAAGAACCTCTGGGTCCAAGGGTAGACCACCAGCAGCCTAAGGGTGGGAA
AATAGACCAATAGGCAGAGAGAGTCAGTGCCTATCAGAAACCCAAGAGTCTTCTCTGTCTCCACATGCCCAGTTTCTAT
TGGTCTCCTTAAACCTGTCTTGTAACCTTGATACCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTT
GCCCCACAGGGCAGTAACGGCAGACTTC

Point Mutation

>E7Mohammadi-HBB3-R sequence exported from A08_E7Mohammadi-HBB3-R_2016-03-17.ab1

NNNNNNNNNNCNNCNNNNTAGGGNGGNNNNNAGANCAATAGGCAGANAGAGNCAGTGCCTATCNNANACNNN
NAGTCTTCTCTGNCTCCACATGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGNAACCTTGATACCAAC
CTGCCCAGGGCCTCACCACCAANTTCNTCNACGTTCACCTTGCCCCACAG

Normal



E8, Homozygous mutation

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

غیر قابل انتقال

۹۵/۲/۵

Preimplantation Genetic Diagnosis

Beta-Thalassemia

✓E8 (Mutated)

Embryo's ID: E8✓
Parents' Mutation: IVSI-6 T>C (c.92+6T>C)
PCR Date: 1394.12.20
Sequencing Date: 1394.12.27

[redacted]
Sampling Date: 1394.12.16
Primer Set: HBB3
Primer Set: HBB3R

Wild Type Sequence:

Point mutation C

GAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCA
AGGTTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGC
ACTGACTCTCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTG
AGTCCTTTGGGGATCTGTCCACTCCTGA

Reverse Complement:

TCAGGAGTGGACAGATCCCCAAAGGACTCAAAGAACCTCTGGGTCCAAGGGTAGACCACCAGCAGCCTAAGGGTGGGAA
AATAGACCAATAGGCAGAGAGAGTCAGTGCCTATCAGAAACCCAAGAGTCTTCTCTGTCTCCACATGCCCAGTTTCTAT
TGGTCTCCTTAAACCTGTCTTGTAACCTTGATACCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTT
GCCCCACAGGGCAGTAACGGCAGACTTC

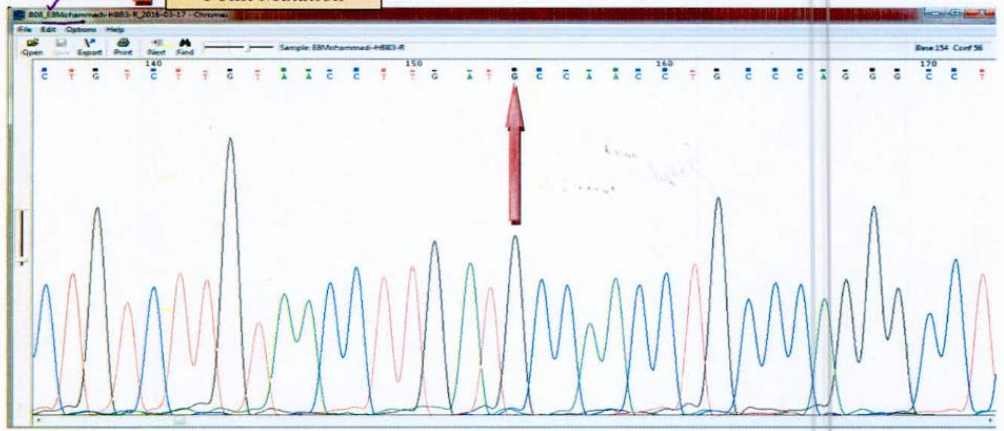
Point Mutation

✓

>E8Mohammadi-HBB3-R sequence exported from B08_E8Mohammadi-HBB3-R_2016-03-17.ab1

NNNNNNNNNNNNNNGGNNNNNCACCAGNNNCCTANGGNGGNNNNNAGACCAATAGGCAGANAGAGTCAGTGC
CTATCANAAACCCAAGAGTCTTCTCTGTCTCCACATGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGT
AACCTTGATCCCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTTGCCCCACAGGNNANNN
NNNNNCAGA

Point Mutation



E9, Homozygous mutation

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

غیرقابل انتقال

۹۵/۲/۵

Preimplantation Genetic Diagnosis

Beta-Thalassemia

E9 (Mutated)

Embryo's ID: E9
Parents' Mutation: IVSI-6 T>C (c.92+6T>C)
PCR Date: 1394.12.20
Sequencing Date: 1394.12.
Sampling Date: 1394.12.16
Primer Set: HBB3
Primer Set: HBB3R

Wild Type Sequence:

Point mutation

GAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGTTGGTATCA
AGGTTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCATGTGGAGACAGAGAAGACTCTTGGGTTTCTGATAGGC
ACTGACTCTCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTG
AGTCCTTTGGGGATCTGTCCACTCCTGA

Reverse Complement:

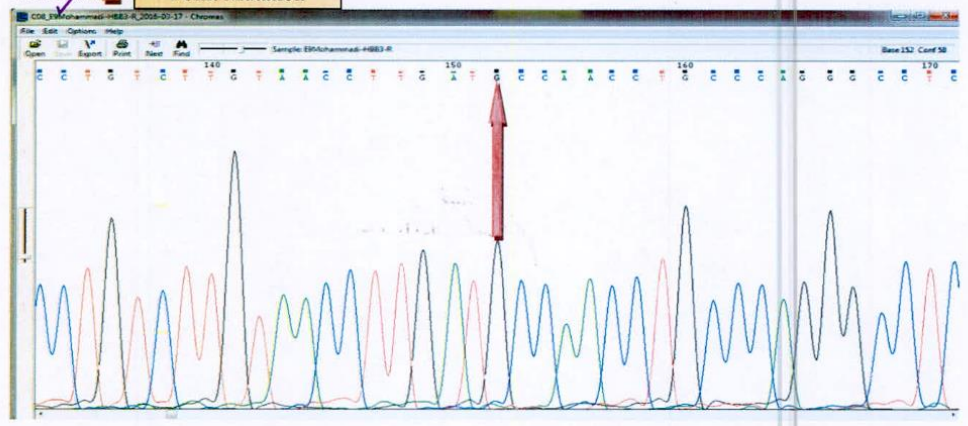
TCAGGAGTGGACAGATCCCCAAAGGACTCAAAGAACCTCTGGGTCCAAGGGTAGACCACCAGCAGCCTAAGGGTGGGAA
AATAGACCAATAGGCAGAGAGAGTCAGTGCCTATCAGAAACCCAAGAGTCTTCTCTGTCTCCACATGCCCAGTTTCTAT
TGGTCTCCTTAAACCTGTCTTGTAACCTTGATACCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTT
GCCCCACAGGGCAGTAACGGCAGACTTC

Point Mutation

>E9Mohammadi-HBB3-R sequence exported from C08_E9Mohammadi-HBB3-R_2016-03-17.ab1

NNNNNNNNNNNNNNNNNNCNCCAGCAGCCTAGGGNGGNNNNNAGACCAATAGGCAGANAGAGTCAGTGCCT
ATCNNANACCCAAGAGTCTTCTCTGTCTCCACATGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAA
CCTTGATCCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTTGCCCCACAGGGNANNANN
NNNCANANN

Point Mutation



مادر و پدر هر دو دارای جهش IVSI-6

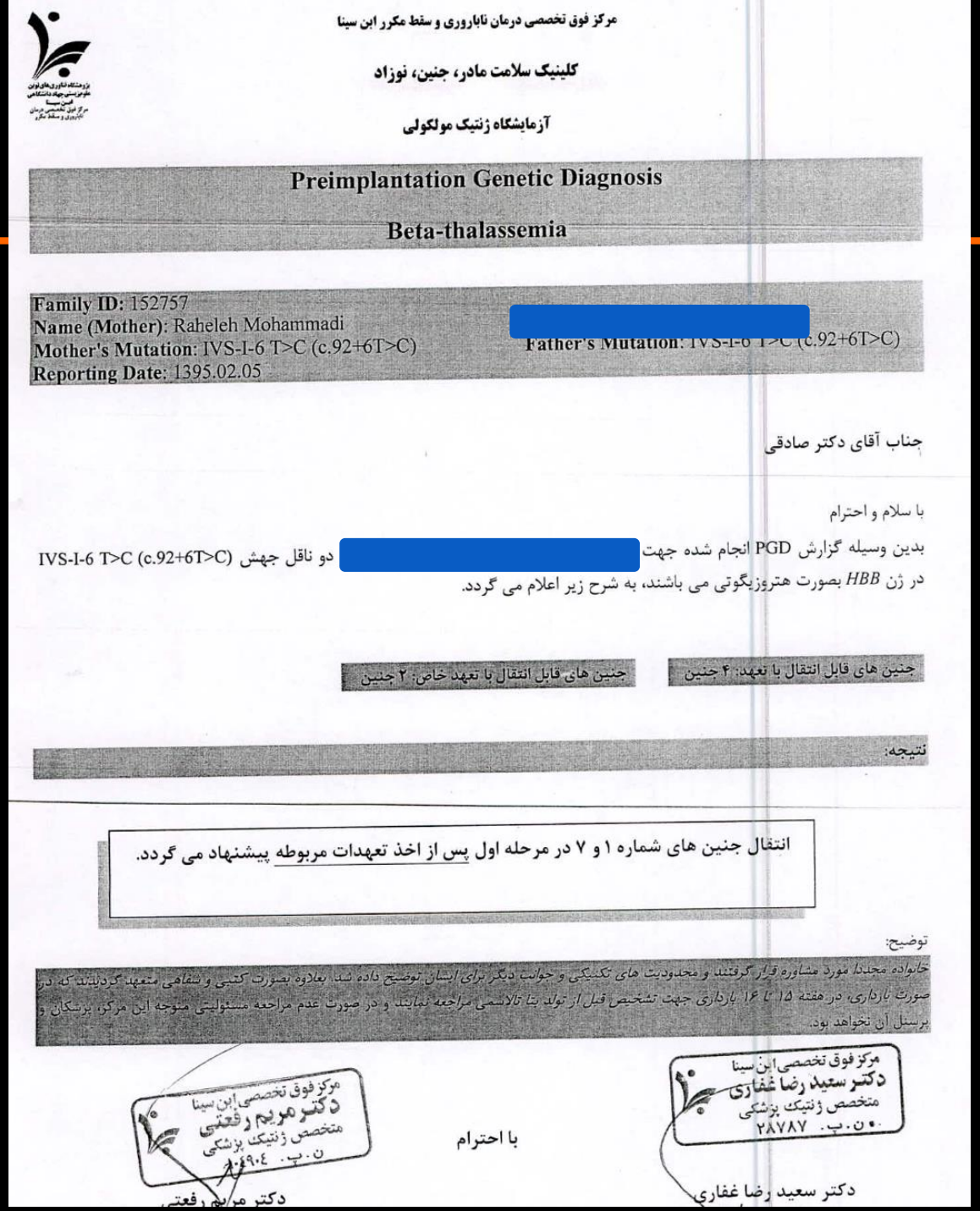
نتایج قید شده در جدول بدون در نظر گرفتن تست رد آلودگی می باشد

Embryos ID	HBB3	HBBN5	Final Result
E1	Normal	Normal	قابل انتقال
E2	Heterozygous	Heterozygous	بدلیل وجود یک شاهد مثبت مبنی بر وجود جهش شاید بهتر باشد با *تعهدنامه ی خاص* انتقال صورت گیرد
E3	به دلیل کیفیت پایین جنین غیرقابل بیوپسی برای بار دوم بوده است		غیر قابل انتقال
E4	* Mutated or Heterozygous	Heterozygous	پیک مربوط به الل wild type در زیر پیک آلل جهش یافته مشخص است ولی دستگاه فقط پیک مربوط به الل جهش یافته را خوانش کرده است.
E5	به دلیل عدم وجود DNA هیچ PCR ی برای آن انجام نشده است		غیر قابل انتقال
E6	Heterozygous	Heterozygous	بدلیل وجود یک شاهد مثبت مبنی بر وجود جهش شاید بهتر باشد با *تعهدنامه ی خاص* انتقال صورت گیرد
E7	Normal	Normal	قابل انتقال
E8	Mutated	Mutated	غیر قابل انتقال
E9	Mutated	Mutated	غیر قابل انتقال
E10	* Mutated or Heterozygous	Mutated Heterozygous	پیک مربوط به الل wild type در زیر پیک آلل جهش یافته مشخص است ولی دستگاه فقط پیک مربوط به الل جهش یافته را خوانش کرده است.

نکته دار

Embryo transfer

First TIME



مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Preimplantation Genetic Diagnosis

Beta-thalassemia

Family ID: 152757
Name (Mother): Raheleh Mohammadi
Mother's Mutation: IVS-I-6 T>C (c.92+6T>C)
[redacted] **Father's Mutation:** IVS-I-6 T>C (c.92+6T>C)
Reporting Date: 1395.02.05

جناب آقای دکتر صادقی

با سلام و احترام

بدین وسیله گزارش PGD انجام شده جهت [redacted] دو ناقل جهش IVS-I-6 T>C (c.92+6T>C) در ژن *HBB* بصورت هتروزیگوتی می باشند، به شرح زیر اعلام می گردد.

جنین های قابل انتقال با تعهد: ۴ جنین

جنین های قابل انتقال با تعهد خاص: ۲ جنین

نتیجه:

انتقال جنین های شماره ۱ و ۷ در مرحله اول پس از اخذ تعهدات مربوطه پیشنهاد می گردد.

توضیح:

خانواده مجددا مورد مشاوره قرار گرفتند و محدودیت های تکنیکی و جواب دیگر برای ایشان توضیح داده شد. بعلاوه بصورت کتبی و شفاهی متعهد گردیدند که در صورت بارداری، در هفته ۱۵ تا ۱۶ بارداری جهت تشخیص قبل از تولد بتا تالاسمی مراجعه نمایند و در صورت عدم مراجعه مسئولیتی متوجه این مرکز، پرسکان و پرسنل آن نخواهد بود.

با احترام

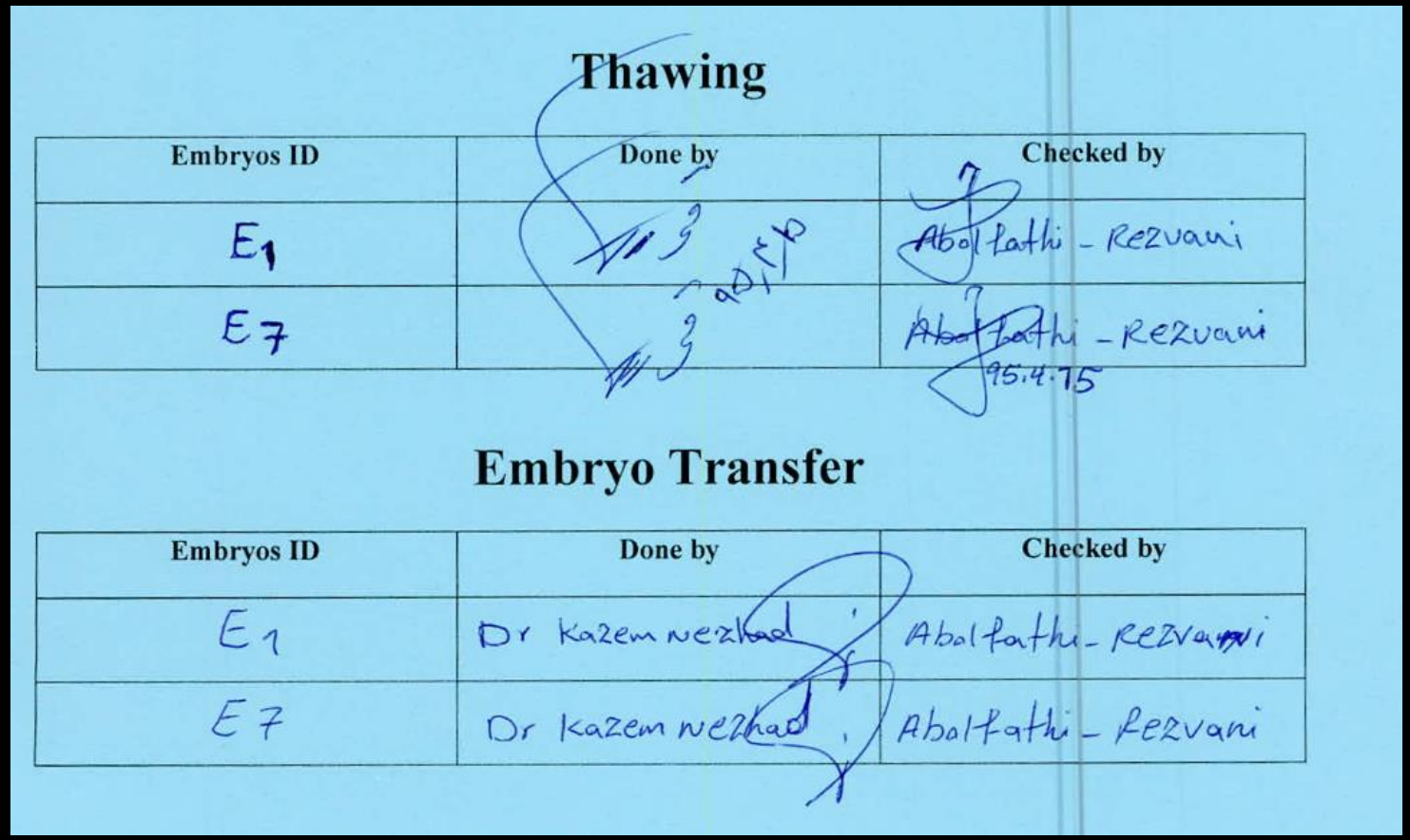
مرکز فوق تخصصی ابن سینا
دکتر سعید رضا غفاری
متخصص ژنتیک پزشکی
ن.ب. ۲۸۷۸۷

دکتر سعید رضا غفاری

مرکز فوق تخصصی ابن سینا
دکتر مریم رفعتی
متخصص ژنتیک پزشکی
ن.ب. ۱۰۰۹۰۴

دکتر مریم رفعتی

Thawing checklist



Thawing

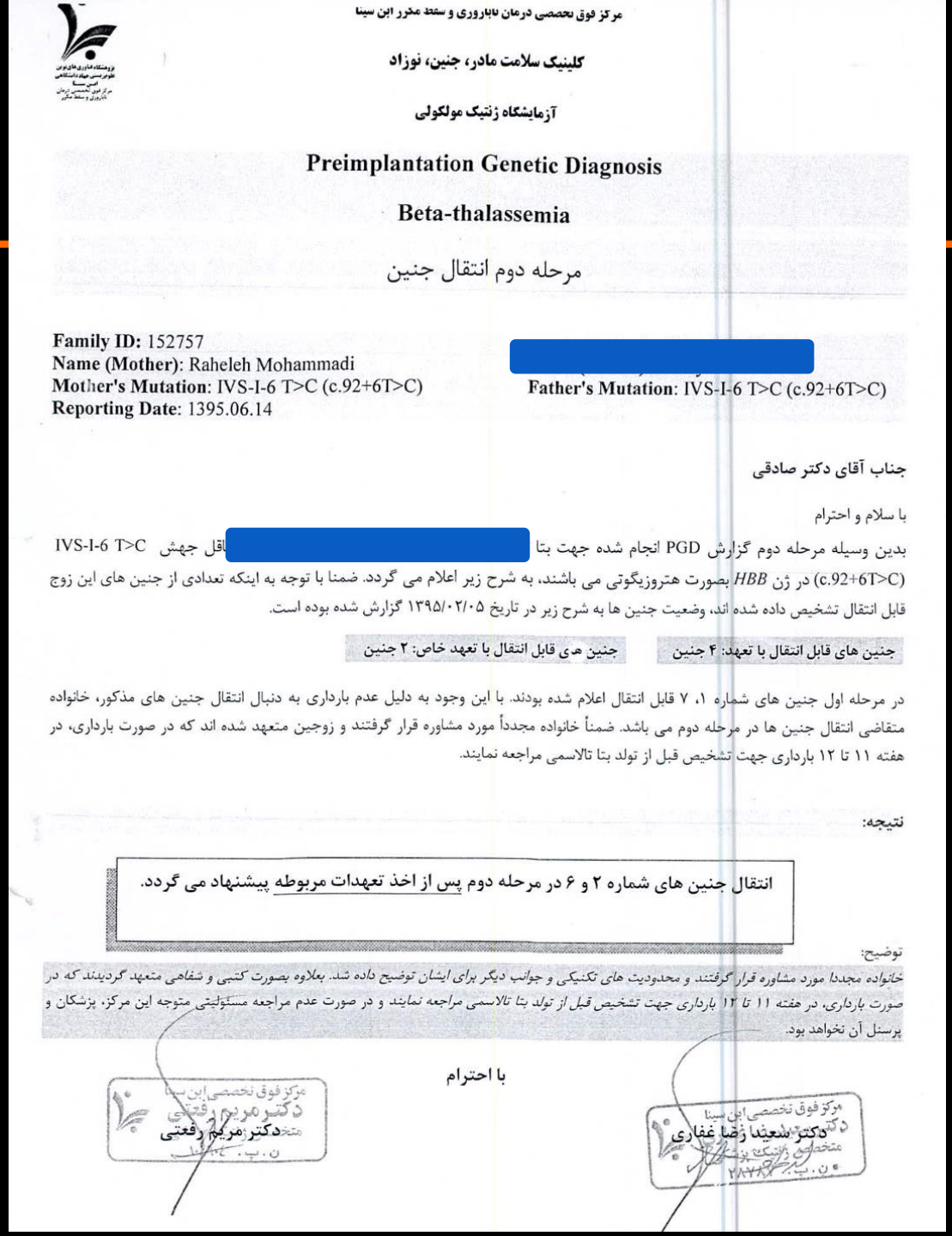
Embryos ID	Done by	Checked by
E1		Abolfathi - Rezvani
E7		Abolfathi - Rezvani 95.4.15

Embryo Transfer

Embryos ID	Done by	Checked by
E1	Dr Kazem Nezhad	Abolfathi - Rezvani
E7	Dr Kazem Nezhad	Abolfathi - Rezvani

Embryo transfer

SECOND TIME



مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا

کلینیک سلامت مادر، جنین، نوزاد

آزمایشگاه ژنتیک مولکولی

Preimplantation Genetic Diagnosis

Beta-thalassemia

مرحله دوم انتقال جنین

Family ID: 152757
Name (Mother): Raheleh Mohammadi
Mother's Mutation: IVS-I-6 T>C (c.92+6T>C)
Reporting Date: 1395.06.14

[redacted]
Father's Mutation: IVS-I-6 T>C (c.92+6T>C)

جناب آقای دکتر صادقی

با سلام و احترام

بدین وسیله مرحله دوم گزارش PGD انجام شده جهت بتا [redacted] ناقل جهش IVS-I-6 T>C (c.92+6T>C) در ژن *HBB* بصورت هتروزیگوتی می باشند، به شرح زیر اعلام می گردد. ضمنا با توجه به اینکه تعدادی از جنین های این زوج قابل انتقال تشخیص داده شده اند، وضعیت جنین ها به شرح زیر در تاریخ ۱۳۹۵/۰۲/۰۵ گزارش شده بوده است.

جنین های قابل انتقال با تعهد: ۴ جنین **جنین های قابل انتقال با تعهد خاص: ۲ جنین**

در مرحله اول جنین های شماره ۱، ۷ قابل انتقال اعلام شده بودند. با این وجود به دلیل عدم بارداری به دنبال انتقال جنین های مذکور، خانواده متقاضی انتقال جنین ها در مرحله دوم می باشد. ضمناً خانواده مجدداً مورد مشاوره قرار گرفتند و زوجین متعهد شده اند که در صورت بارداری، در هفته ۱۱ تا ۱۲ بارداری جهت تشخیص قبل از تولد بتا تالاسمی مراجعه نمایند.

نتیجه:

انتقال جنین های شماره ۲ و ۶ در مرحله دوم پس از اخذ تعهدات مربوطه پیشنهاد می گردد.

توضیح:

خانواده مجددا مورد مشاوره قرار گرفتند و محدودیت های تکنیکی و جوانب دیگر برای ایشان توضیح داده شد. بعلاوه بصورت کتبی و شفاهی متعهد گردیدند که در صورت بارداری، در هفته ۱۱ تا ۱۲ بارداری جهت تشخیص قبل از تولد بتا تالاسمی مراجعه نمایند و در صورت عدم مراجعه مسئولیتی متوجه این مرکز، پزشکان و پرسنل آن نخواهد بود.

با احترام

مرکز فوق تخصصی ابن سینا
دکتر مریم رفعتی
متخصص ژنتیک پزشکی
ن. ب. [redacted]

دکتر مریم رفعتی

مرکز فوق تخصصی ابن سینا
دکتر سعیدا رضا غفاری
متخصص ژنتیک پزشکی
ن. ب. [redacted]

دکتر سعیدا رضا غفاری

Family ID: 152757
Name (Moth [redacted] **Name (Fath** [redacted]
Mother's Mutation: IVS-I-6 T>C(c.92+6T>C **Father's Mutation:** IVS-I-6 T>C(c.92+6T>C)
Date of Embryo Transfer: 95.7.24

Thawing

Embryos ID	Done by	Checked by
2	Fathi	Rezvani, Barati 95.7.24
6	Fathi	Rezvani - Barati 95.7.24

Embryo Transfer

Embryos ID	Done by	Checked by
2	Dr. Kazemi Nezhad	Rezvani Barati
6	Dr. kazemi Nezhad	Rezvani - Barati

Embryo transfer
THIRD TIME

- Transfer date: Ordibehesht 1396, May 2017
- The mother got pregnant!

PND

- The fetus was unaffected
- Compatible PND and PGT-M results

مرکز فوق تخصصی درمان ناباروری و سقط مکرر ابن سینا
کلینیک سلامت مادر، جنین، نوزاد
آزمایشگاه ژنتیک مولکولی

Molecular Genetic Analysis Report

[redacted]

HBB Mutation Analysis
Prenatal Diagnosis

Report Continued from the Previous Page

Results:
The results of the genetic investigation of the parents and the fetal sample are shown in the below table.

ID	Mutation Investigated
	IVSI-6 T>C (c.92+6T>C)
Raheleh Mohammadi (Mother)	Heterozygous
Ali Eyni (Father)	Heterozygous
Fetal Sample (CVS)	Heterozygous

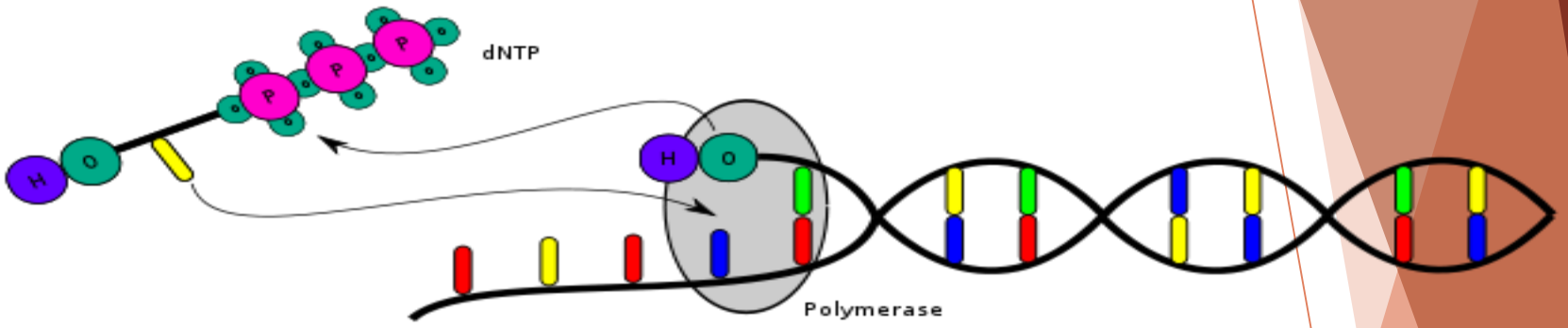
Comments and Recommendations: This study Shows that the fetus has received one mutant allele (heterozygous for c.92+6T>C mutation) and therefore, is a carrier of beta thalassemia. Other genetic and non-genetic disorders outside the regions studied have not been investigated in this study. Prenatal diagnosis is highly recommended in all possible future pregnancy.

Signed:

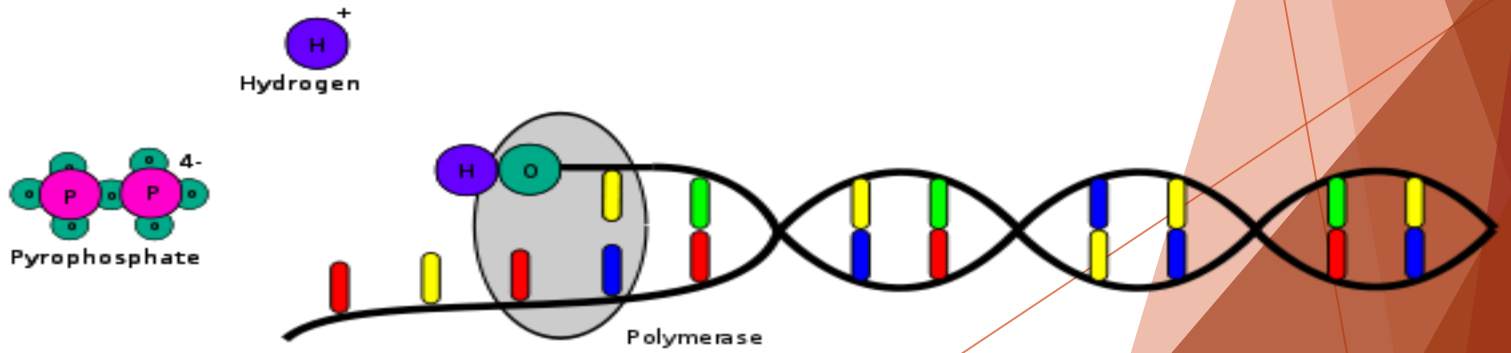
PGT-A and PGT-SR using next-generation sequencing

Platform: Ion Torrent

Basics

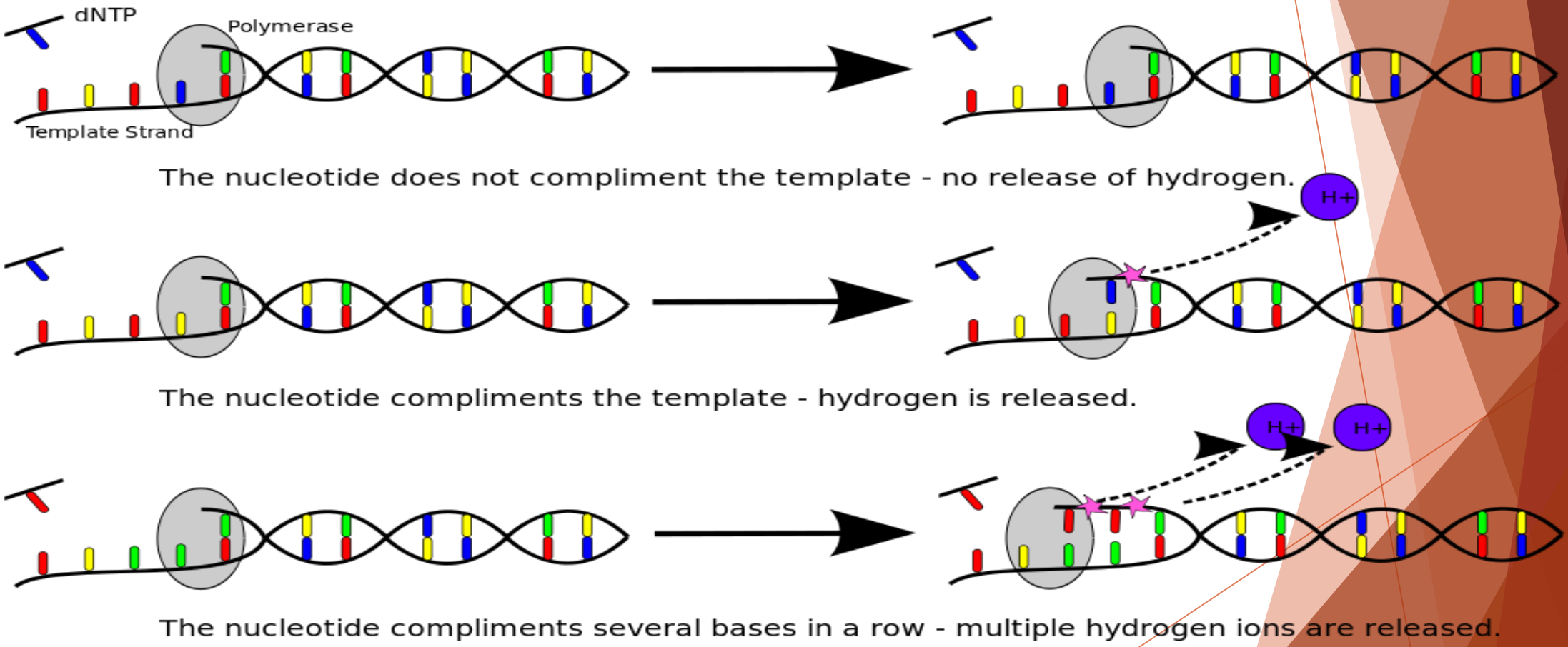


Polymerase integrates a nucleotide.

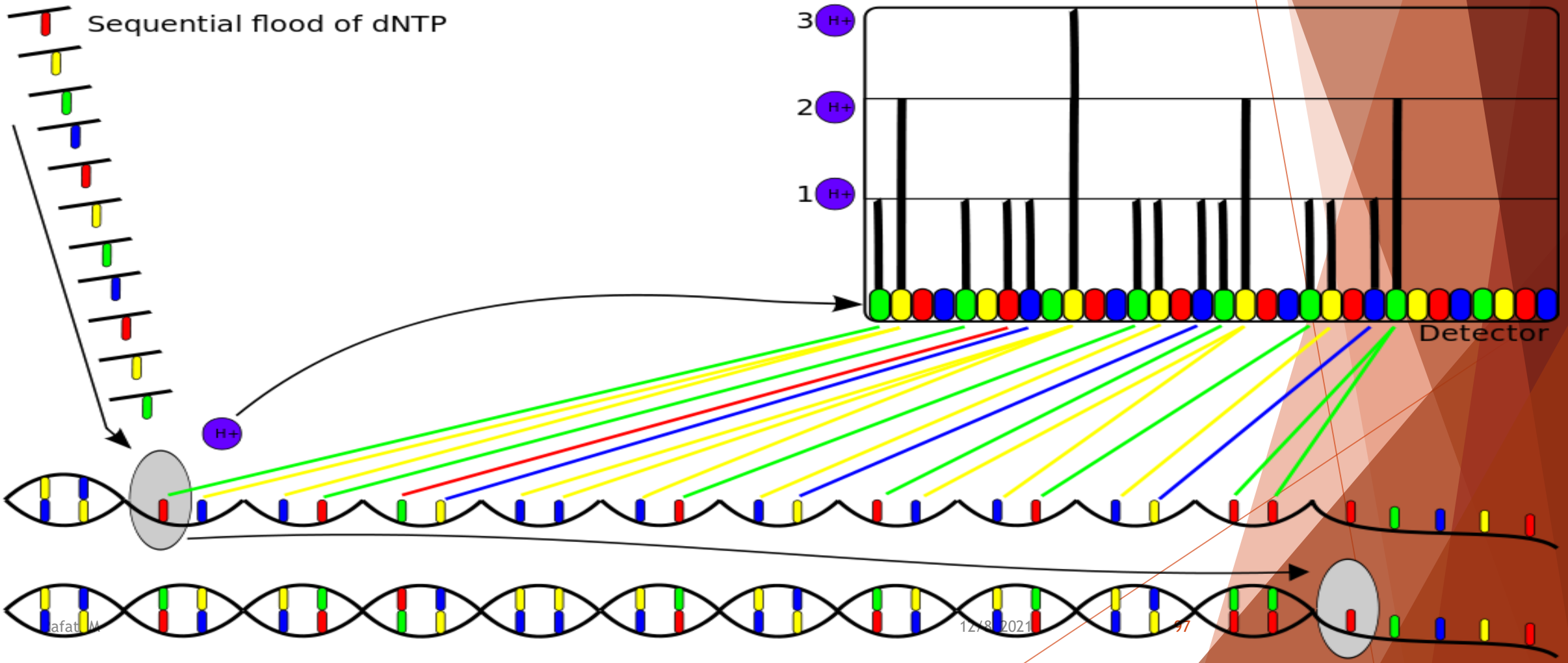


Hydrogen and pyrophosphate are released.

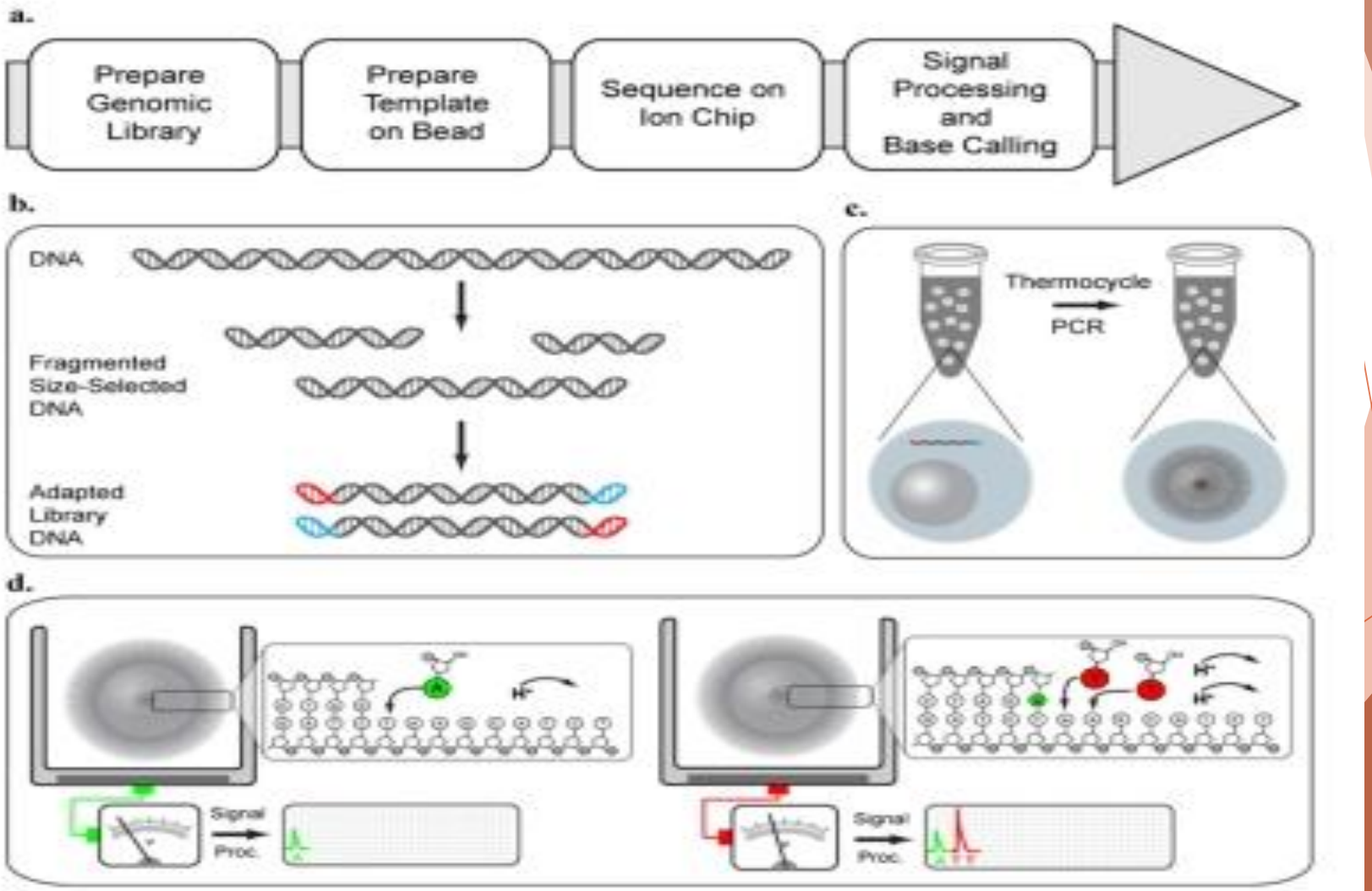
Basics


dNTP
Polymerase
Template Strand
The nucleotide does not compliment the template - no release of hydrogen.
H+
The nucleotide compliments the template - hydrogen is released.
H+
H+
The nucleotide compliments several bases in a row - multiple hydrogen ions are released.

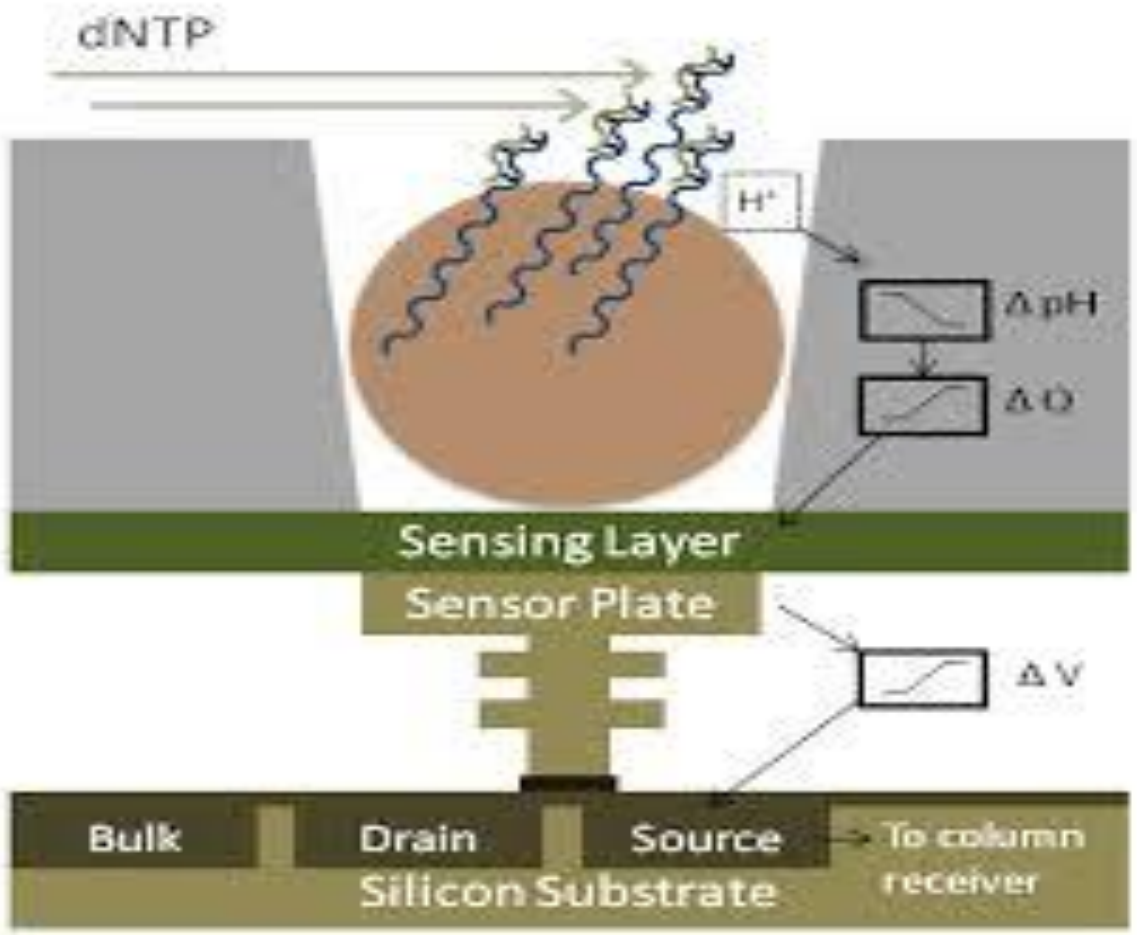
Basics

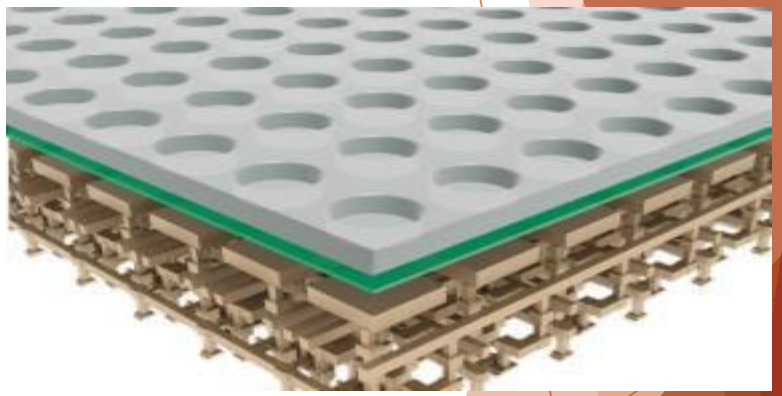


Basics

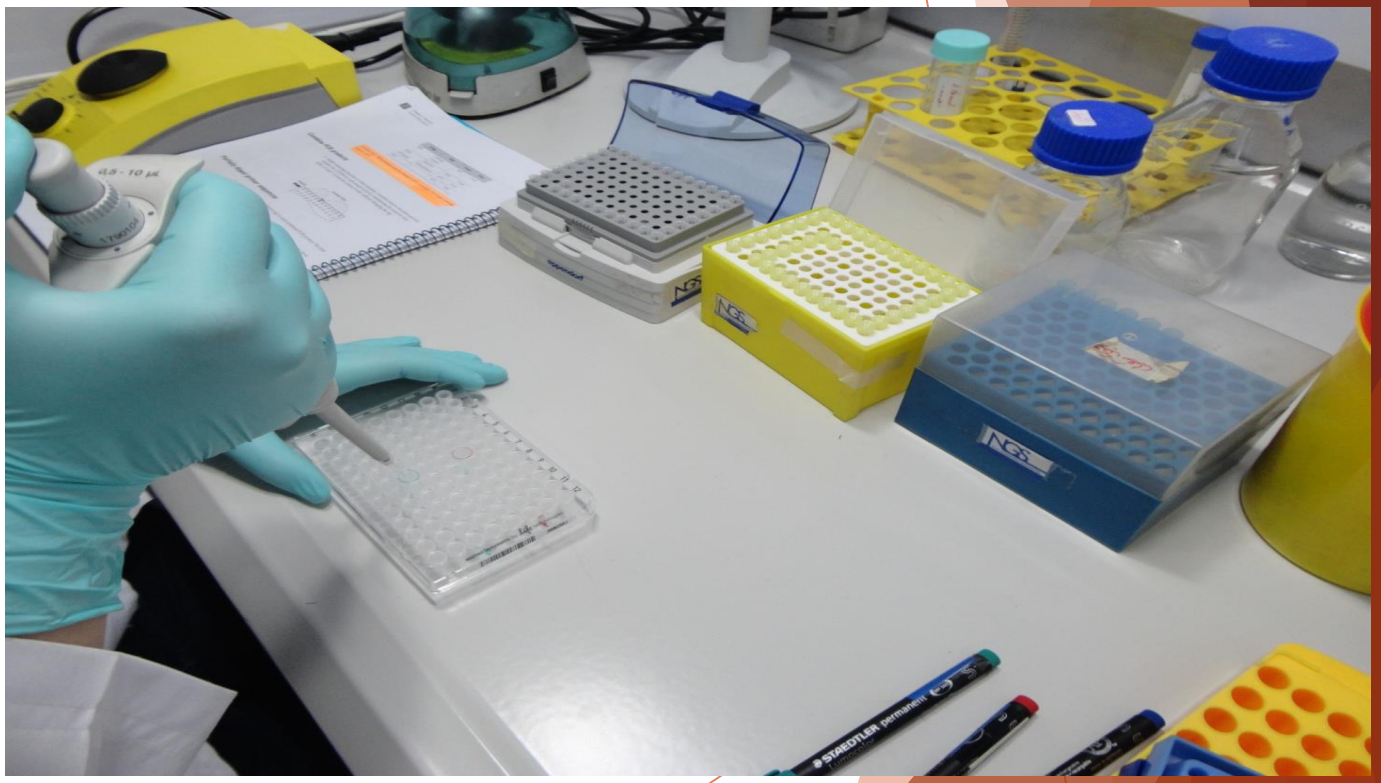

a.
Prepare Genomic Library
Prepare Template on Bead
Sequence on Ion Chip
Signal Processing and Base Calling
b.
DNA
Fragmented Size-Selected DNA
Adapted Library DNA
c.
Thermocycle
PCR
d.
Signal Proc.
Signal Proc.

Basics


dNTP
H+
ΔpH
ΔO
Sensing Layer
Sensor Plate
ΔV
Bulk
Drain
Source
To column receiver
Silicon Substrate

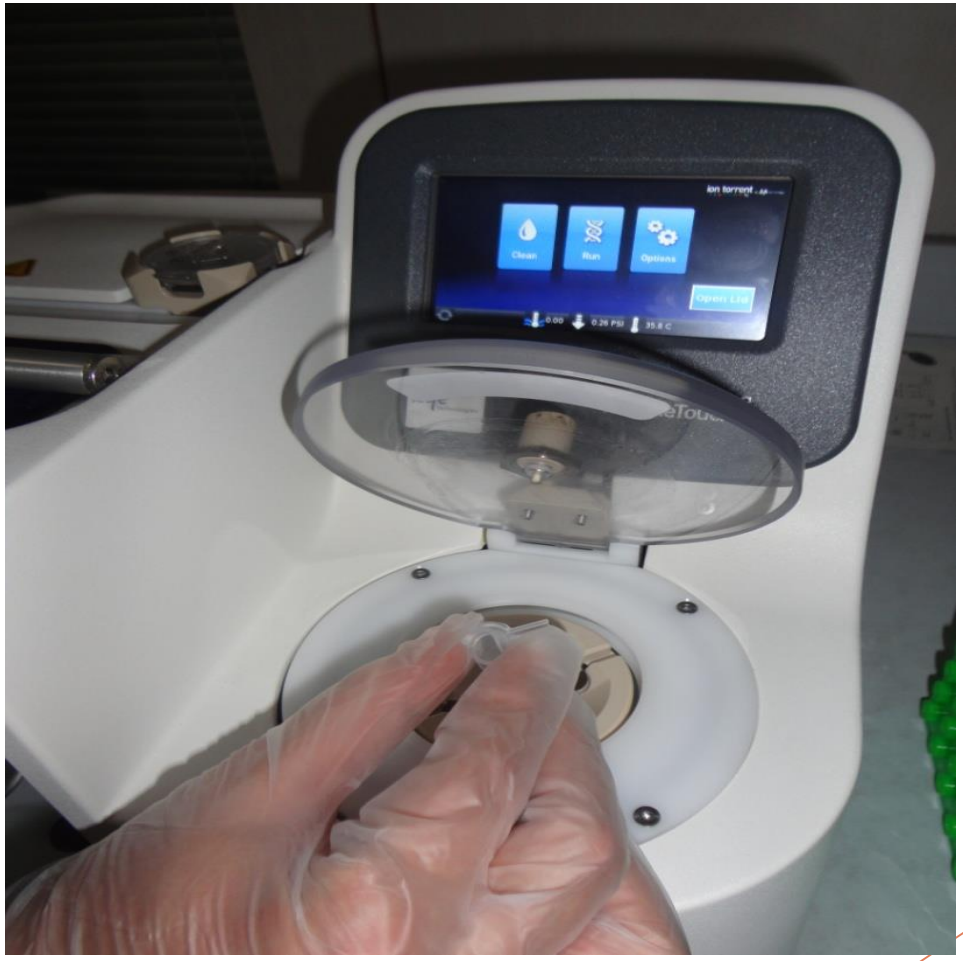


Library Preparation

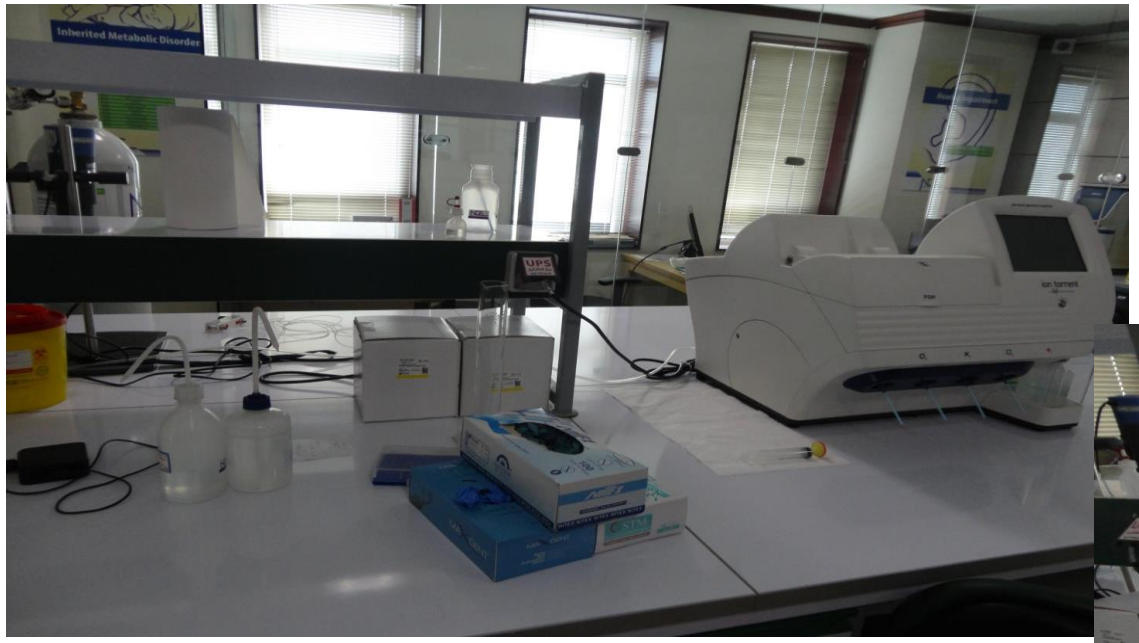


Size selection

Template Preparation



Sequencing, PGM

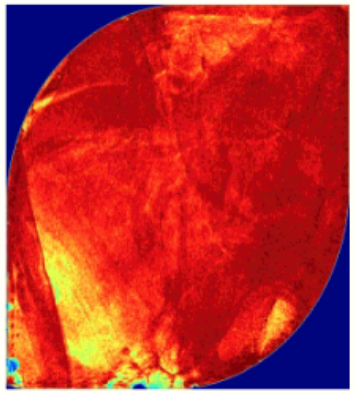


768 M
Total Bases

63
Key Signal

90 %
ISP Loading

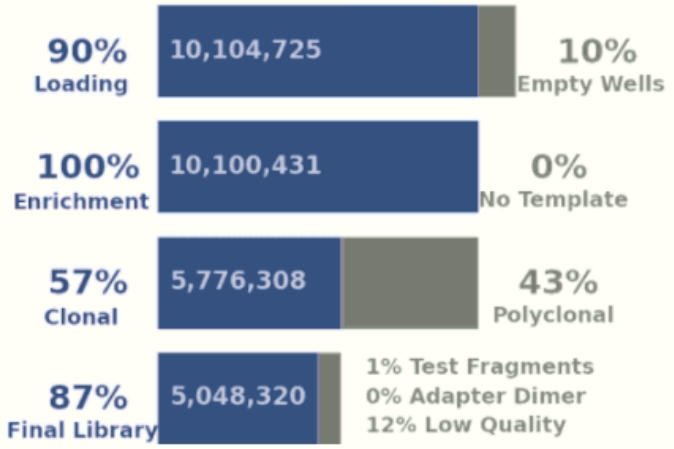
ISP Density



5,048,320
Total Reads

50 %
Usable Reads

ISP Summary

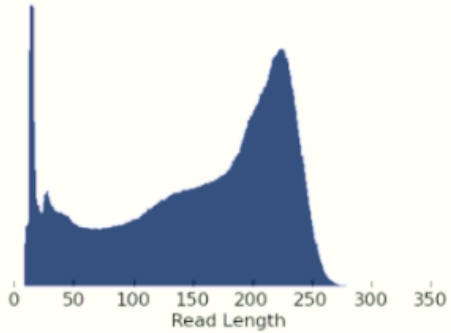


152 bp
Mean

172 bp
Median

14 bp
Mode

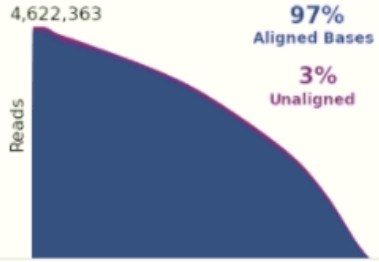
Read Length



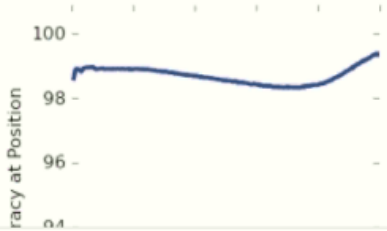
Aligned to Homo sapiens

722 M
Total Aligned Bases

0.2X
Reference Coverage



98.7%
Mean Raw Accuracy 1x



648 M
AQ17 Total Bases

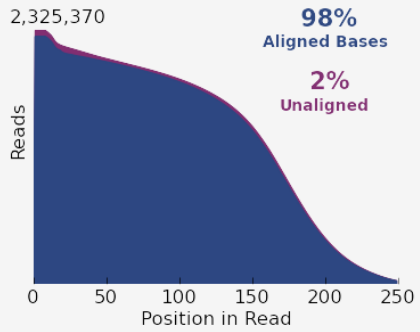
Alignment Quality

	AQ17	AQ20	Perfe
Total Number of Bases [bp]	648 M	561 M	415 M
Mean Length [bp]	160	145	111
Longest Alignment [bp]	319	319	308
Mean Coverage Depth [x]	0.2	0.2	0.1

213.140.138.244/report/1/

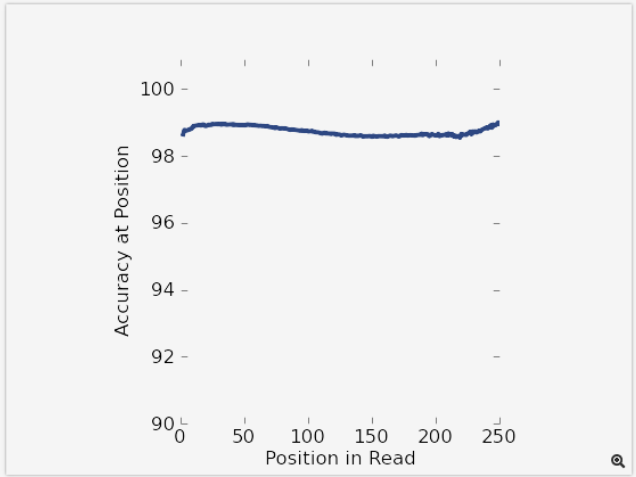
339 M
Total Aligned Bases

0.1X
Reference Coverage



	Count	%
Total Reads	2,325,370	—
Aligned Reads	2,270,251	97.6%
Unaligned Reads	55,119	2.4%

98.8%
Mean Raw Accuracy 1x



305 M
AQ17 Total Bases

Alignment Quality

	AQ17	AQ20	Perfect
Total Number of Bases [bp]	305 M	275 M	220 M
Mean Length [bp]	156	146	121
Longest Alignment [bp]	296	293	285
Mean Coverage Depth [x]	0.1	0.1	0.1

variantCaller (v4.2.1.0) variantCaller.html — Error

No plugin output at this time.

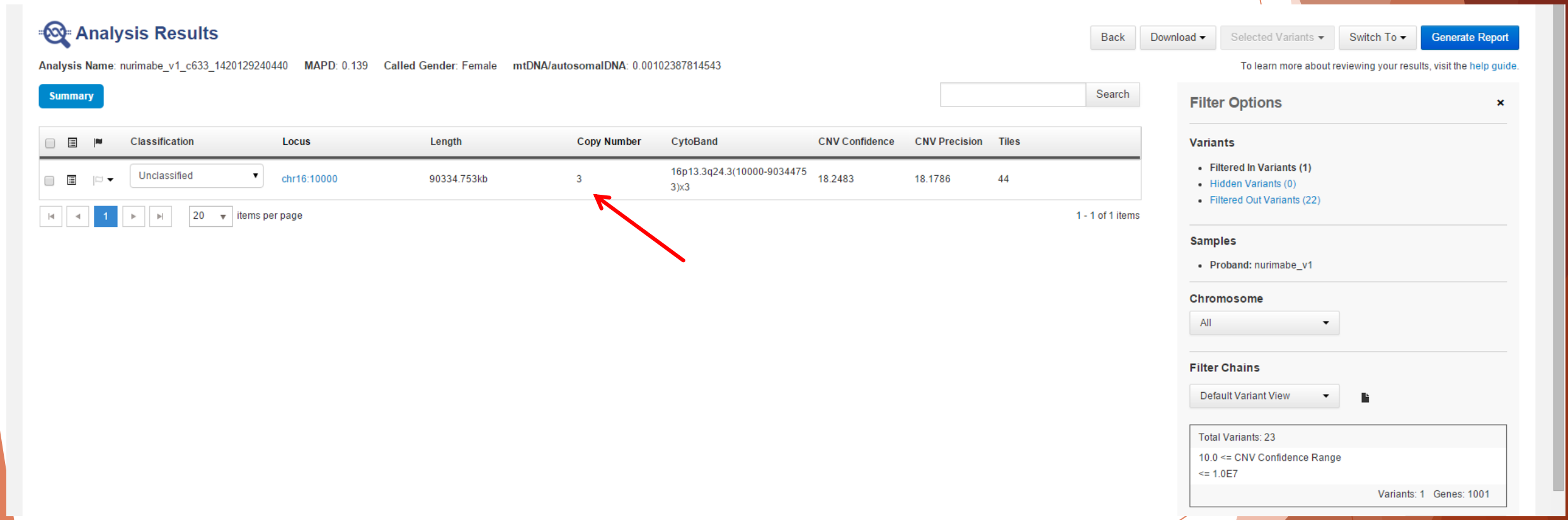
variantCaller (v4.2.1.0) variantCaller.html — Error

No plugin output at this time.

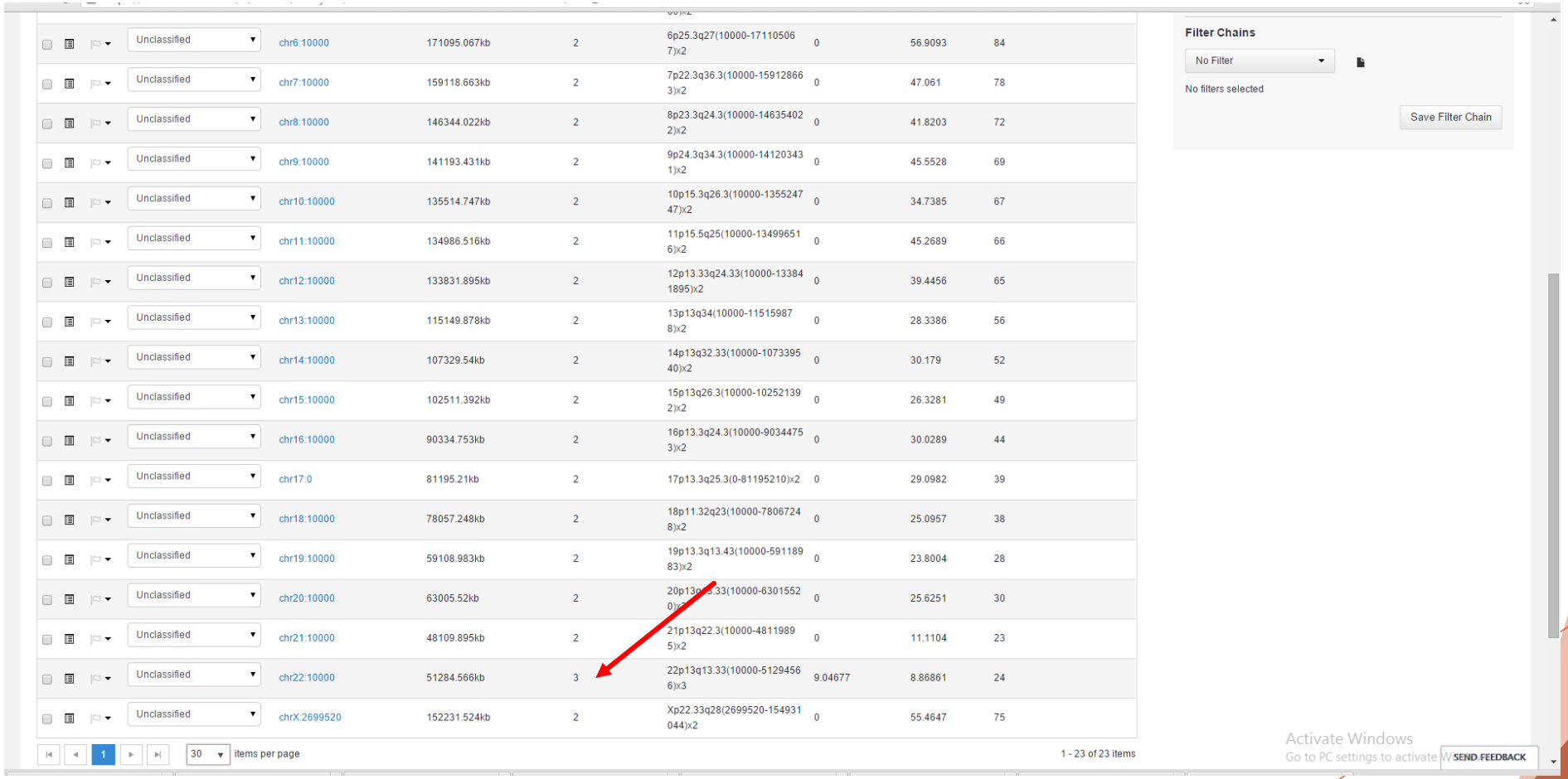
213.140.138.244/report/1/#rawAccuracyModal

Optimization Phase

Product of conception: Trisomy of chromosome 16



Product of conception: Trisomy of chromosome 22



Unclassified	chr6:10000	171095.067kb	2	6p25.3q27(10000-171105067)x2	0	56.9093	84
Unclassified	chr7:10000	159118.663kb	2	7p22.3q36.3(10000-159128663)x2	0	47.061	78
Unclassified	chr8:10000	146344.022kb	2	8p23.3q24.3(10000-146354022)x2	0	41.8203	72
Unclassified	chr9:10000	141193.431kb	2	9p24.3q34.3(10000-141203431)x2	0	45.5528	69
Unclassified	chr10:10000	135514.747kb	2	10p15.3q26.3(10000-135524747)x2	0	34.7385	67
Unclassified	chr11:10000	134986.516kb	2	11p15.5q25(10000-134996516)x2	0	45.2689	66
Unclassified	chr12:10000	133831.895kb	2	12p13.33q24.33(10000-133841895)x2	0	39.4456	65
Unclassified	chr13:10000	115149.878kb	2	13p13q34(10000-115159878)x2	0	28.3386	56
Unclassified	chr14:10000	107329.54kb	2	14p13q32.33(10000-107339540)x2	0	30.179	52
Unclassified	chr15:10000	102511.392kb	2	15p13q26.3(10000-102521392)x2	0	26.3281	49
Unclassified	chr16:10000	90334.753kb	2	16p13.3q24.3(10000-90344753)x2	0	30.0289	44
Unclassified	chr17:0	81195.21kb	2	17p13.3q25.3(0-81195210)x2	0	29.0982	39
Unclassified	chr18:10000	78057.248kb	2	18p11.32q23(10000-78067248)x2	0	25.0957	38
Unclassified	chr19:10000	59108.983kb	2	19p13.3q13.43(10000-59118983)x2	0	23.8004	28
Unclassified	chr20:10000	63005.52kb	2	20p13q13.33(10000-63015520)x2	0	25.6251	30
Unclassified	chr21:10000	48109.895kb	2	21p13q22.3(10000-48119895)x2	0	11.1104	23
Unclassified	chr22:10000	51284.566kb	3	22p13q13.33(10000-51294566)x3	9.04677	8.86861	24
Unclassified	chrX:2699520	152231.524kb	2	Xp22.33q28(2699520-154931044)x2	0	55.4647	75

1 30 items per page 1 - 23 of 23 items

Filter Chains

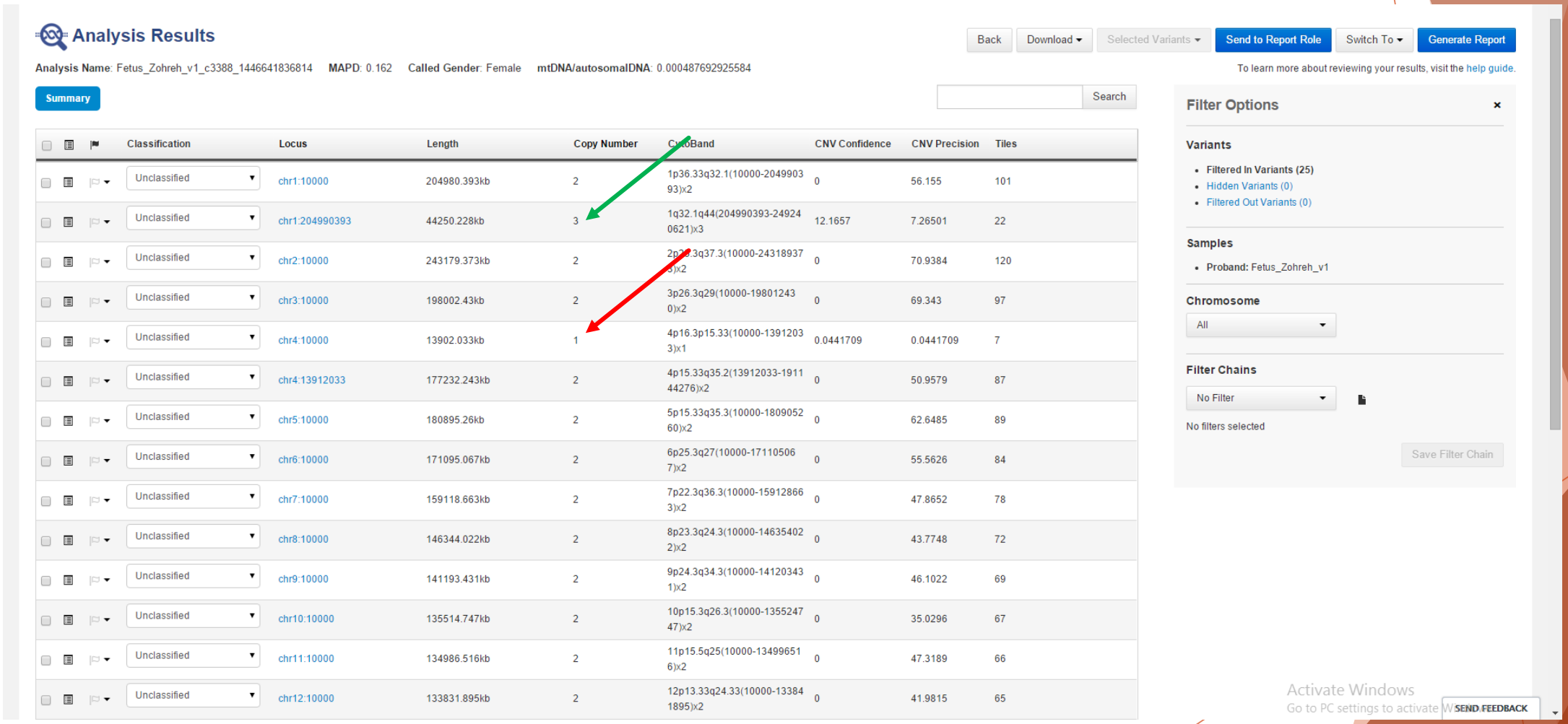
No Filter

No filters selected

Save Filter Chain

Detection of an unbalanced chromosome abnormality

Partial trisomy of 1q
partial monosomy of 4p



Analysis Results

Back | Download | Selected Variants | Send to Report Role | Switch To | Generate Report

Analysis Name: Fetus_Zohreh_v1_c3388_1446641836814 MAPD: 0.162 Called Gender: Female mtDNA/autosomalDNA: 0.000487692925584

To learn more about reviewing your results, visit the help guide.

Summary

Search

Classification	Locus	Length	Copy Number	CytoBand	CNV Confidence	CNV Precision	Tiles
Unclassified	chr1:10000	204980.393kb	2	1p36.33q32.1(10000-204990393)x2	0	56.155	101
Unclassified	chr1:204990393	44250.228kb	3	1q32.1q44(204990393-249240621)x3	12.1657	7.26501	22
Unclassified	chr2:10000	243179.373kb	2	2p25.3q37.3(10000-243189375)x2	0	70.9384	120
Unclassified	chr3:10000	198002.43kb	2	3p26.3q29(10000-198012430)x2	0	69.343	97
Unclassified	chr4:10000	13902.033kb	1	4p16.3p15.33(10000-13912033)x1	0.0441709	0.0441709	7
Unclassified	chr4:13912033	177232.243kb	2	4p15.33q35.2(13912033-191144276)x2	0	50.9579	87
Unclassified	chr5:10000	180895.26kb	2	5p15.33q35.3(10000-180905260)x2	0	62.6485	89
Unclassified	chr6:10000	171095.067kb	2	6p25.3q27(10000-171105067)x2	0	55.5626	84
Unclassified	chr7:10000	159118.663kb	2	7p22.3q36.3(10000-159128663)x2	0	47.8652	78
Unclassified	chr8:10000	146344.022kb	2	8p23.3q24.3(10000-146354022)x2	0	43.7748	72
Unclassified	chr9:10000	141193.431kb	2	9p24.3q34.3(10000-141203431)x2	0	46.1022	69
Unclassified	chr10:10000	135514.747kb	2	10p15.3q26.3(10000-135524747)x2	0	35.0296	67
Unclassified	chr11:10000	134986.516kb	2	11p15.5q25(10000-134996516)x2	0	47.3189	66
Unclassified	chr12:10000	133831.895kb	2	12p13.33q24.33(10000-133841895)x2	0	41.9815	65

Filter Options

Variants
- Filtered In Variants (25)
- Hidden Variants (0)
- Filtered Out Variants (0)

Samples
- Proband: Fetus_Zohreh_v1

Chromosome
All

Filter Chains
No Filter

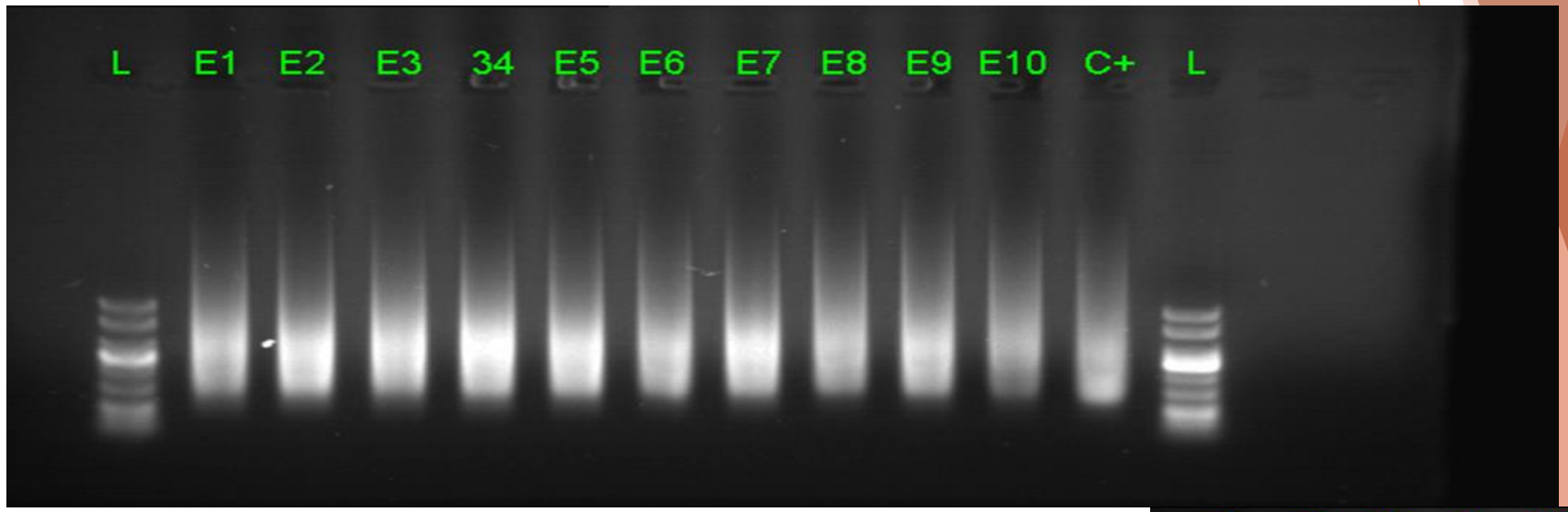
No filters selected

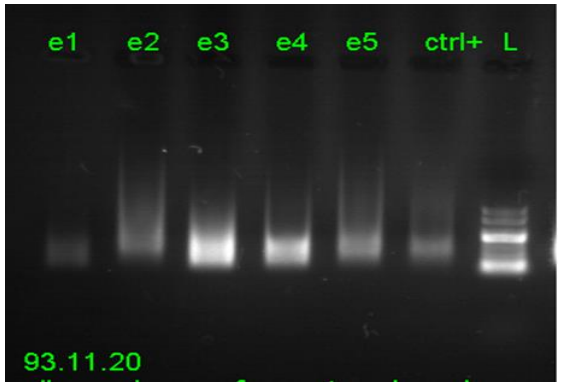
Save Filter Chain

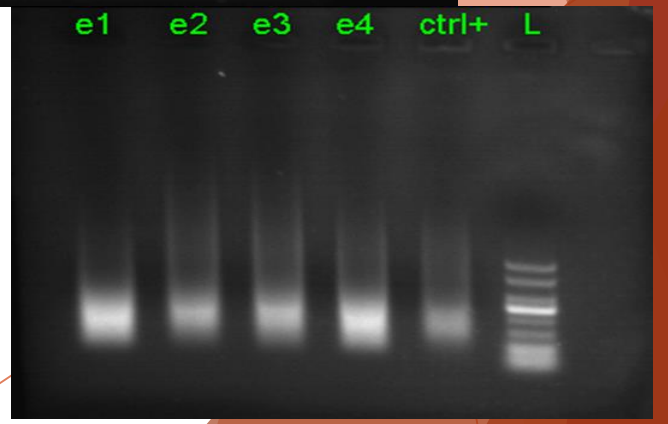
Activate Windows
Go to PC settings to activate W

SEND FEEDBACK

Whole Genome Amplification







Normal embryo

Unclassified	chr2:10000	243179.373kb	2	2p25.3q37.3(10000-243189373)x2	0	46.3702	120
Unclassified	chr3:10000	198002.43kb	2	3p26.3q29(10000-198012430)x2	0	42.3559	97
Unclassified	chr4:10000	191134.276kb	2	4p16.3q35.2(10000-191144276)x2	0	59.694	94
Unclassified	chr5:10000	180895.26kb	2	5p15.33q35.3(10000-180905260)x2	0	67.8996	89
Unclassified	chr6:10000	171095.067kb	2	6p25.3q27(10000-171105067)x2	0	39.7758	84
Unclassified	chr7:10000	159118.663kb	2	7p22.3q36.3(10000-159128663)x2	0	30.721	78
Unclassified	chr8:10000	146344.022kb	2	8p23.3q24.3(10000-146354022)x2	0	41.8521	72
Unclassified	chr9:10000	141193.431kb	2	9p24.3q34.3(10000-141203431)x2	0	17.8583	69
Unclassified	chr10:10000	135514.747kb	2	10p15.3q26.3(10000-135524747)x2	0	31.5015	67
Unclassified	chr11:10000	134986.516kb	2	11p15.5q25(10000-134996516)x2	0	21.3909	66
Unclassified	chr12:10000	133831.895kb	2	12p13.33q24.33(10000-133841895)x2	0	21.9966	65
Unclassified	chr13:10000	115149.878kb	2	13p13q34(10000-115159878)x2	0	30.8793	56
Unclassified	chr14:10000	107329.54kb	2	14p13q32.33(10000-107339540)x2	0	8.53804	52
Unclassified	chr15:10000	102511.392kb	2	15p13q26.3(10000-102521392)x2	0	10.2424	49
Unclassified	chr16:10000	90334.753kb	2	16p13.3q24.3(10000-90344753)x2	0	15.0169	44
Unclassified	chr17:0	81195.21kb	2	17p13.3q25.3(0-81195210)x2	0	01	39
Unclassified	chr18:10000	78057.248kb	2	18p11.32q23(10000-78067248)x2	0	27.4368	38
Unclassified	chr19:10000	59108.983kb	2	19p13.3q13.43(10000-59118983)x2	0	9.89214	28
Unclassified	chr20:10000	63005.52kb	2	20p13q13.33(10000-63015520)x2	0	22.1778	30

16p13.3q24.3(10000-90344753)x2

Samples

- **Proband:** Embryo_Rahmani_v1

Chromosome

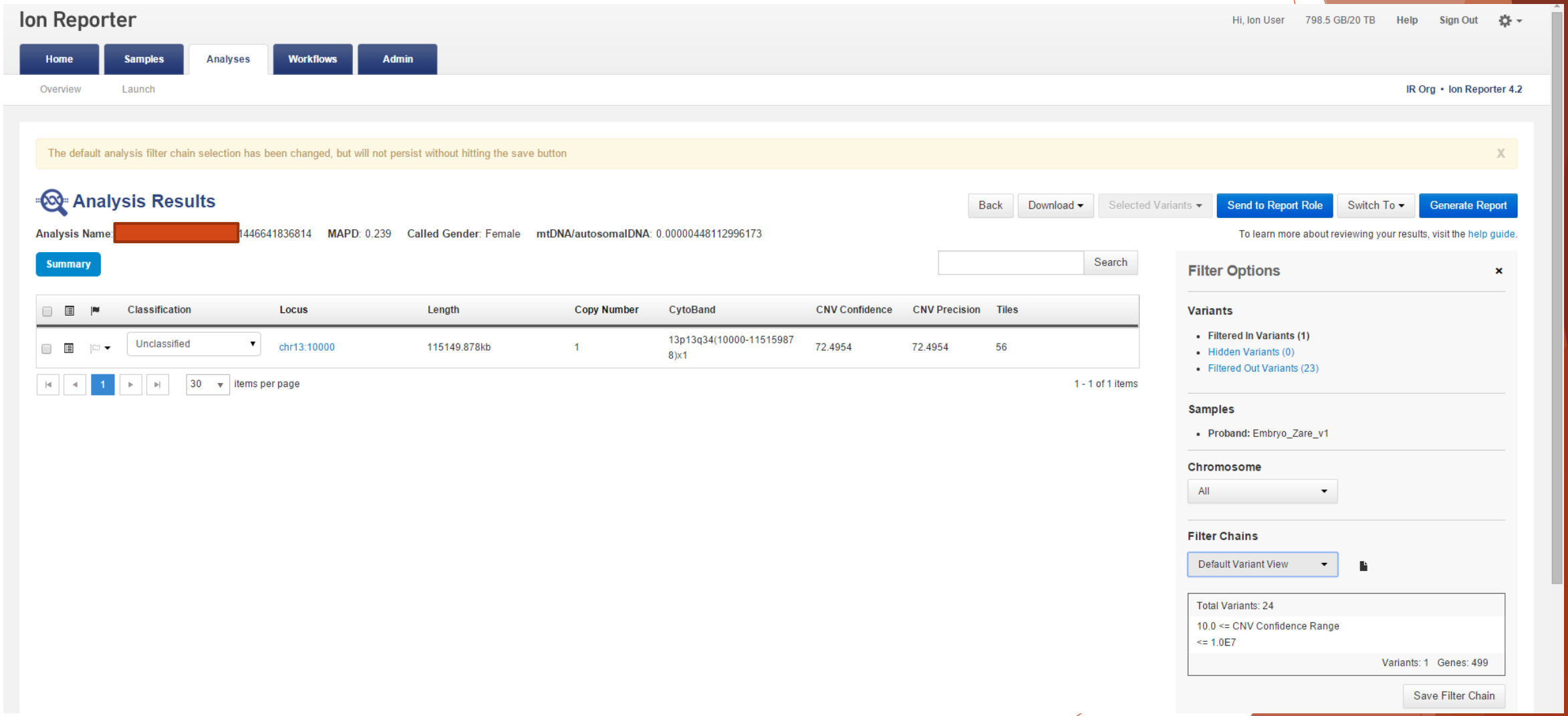
All

Filter Chains

No Filter

No filters selected

PGS-NGS
Monosomy of chromosome 13



Gender: Female

Unclassified	chr12:37856694	95985.201kb	2	12q11q24.33(37856694-133841895)x2	0	31.4368	48
Unclassified	chr13:10000	115149.878kb	1	13p13q34(10000-115159878)x1	72.4954	72.4954	56
Unclassified	chr14:10000	107329.54kb	2	14p13q32.33(10000-107339540)x2	0	18.2322	52
Unclassified	chr15:10000	102511.392kb	2	15p13q26.3(10000-102521392)x2	0	11.776	49
Unclassified	chr16:10000	90334.753kb	2	16p13.3q24.3(10000-90344753)x2	0	32.2727	44
Unclassified	chr17:0	81195.21kb	2	17p13.3q25.3(0-81195210)x2	0	29.3956	39
Unclassified	chr18:10000	78057.248kb	2	18p11.32q23(10000-78067248)x2	0	23.0054	38
Unclassified	chr19:10000	59108.983kb	2	19p13.3q13.43(10000-59118983)x2	0	14.6514	28
Unclassified	chr20:10000	63005.52kb	2	20p13q13.33(10000-63015520)x2	0	22.6232	30
Unclassified	chr21:10000	48109.895kb	2	21p13q22.3(10000-48119895)x2	0	16.9951	23
Unclassified	chr22:10000	51284.566kb	2	22p13q13.33(10000-51294566)x2	0	12.4714	24
Unclassified	chrX:2699520	152231.524kb	2	Xp22.33q28(2699520-154931044)x2	0	30.4022	75

1 30 items per page 1 - 24 of 24 items

Post-Analysis Plugins

Gender: Male

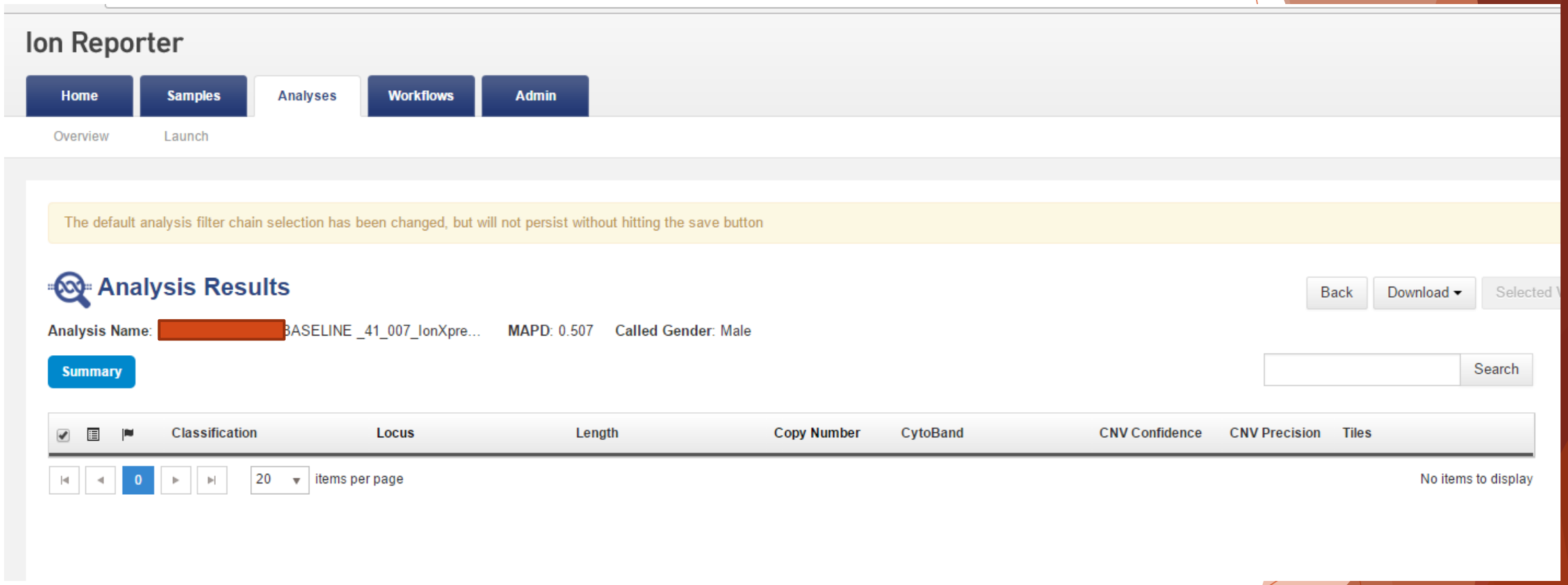
Unclassified	chr8:10000	146344.022kb	2	8p23.3q24.3(10000-146354022)x2	0	28.592	72
Unclassified	chr9:10000	141193.431kb	2	9p24.3q34.3(10000-141203431)x2	0	33.0527	69
Unclassified	chr10:10000	135514.747kb	2	10p15.3q26.3(10000-135524747)x2	0	27.8227	67
Unclassified	chr11:10000	134986.516kb	2	11p15.5q25(10000-134996516)x2	0	34.0387	66
Unclassified	chr12:10000	133831.895kb	2	12p13.33q24.33(10000-133841895)x2	0	29.0351	65
Unclassified	chr13:10000	115149.878kb	2	13p13q34(10000-115159878)x2	0	19.7638	56
Unclassified	chr14:10000	107329.54kb	2	14p13q32.33(10000-107339540)x2	0	23.1274	52
Unclassified	chr15:10000	102511.392kb	2	15p13q26.3(10000-102521392)x2	0	23.2512	49
Unclassified	chr16:10000	90334.753kb	2	16p13.3q24.3(10000-90344753)x2	0	20.2768	44
Unclassified	chr17:0	81195.21kb	2	17p13.3q25.3(0-81195210)x2	0	19.3581	39
Unclassified	chr18:10000	78057.248kb	2	18p11.32q23(10000-78067248)x2	0	17.7867	38
Unclassified	chr19:10000	59108.983kb	2	19p13.3q13.43(10000-59118983)x2	0	10.4512	28
Unclassified	chr20:10000	63005.52kb	2	20p13q13.33(10000-63015520)x2	0	16.6322	30
Unclassified	chr21:10000	48109.895kb	2	21p13q22.3(10000-48119895)x2	0	6.83962	23
Unclassified	chr22:10000	51284.566kb	2	22p13q13.33(10000-51294566)x2	0	7.40116	24
Unclassified	chrX:2699520	152231.524kb	1	Xp22.33q28(2699520-154931044)x1	0	143.723	75
Unclassified	chrY:2649520	56160.48kb	1	Yp11.31q12(2649520-58810000)x1	0	16.8821	26

1 30 items per page

1 - 24 of 24 items

Clinical Phase

NL Male E3 OSK



NL Male, E1 SEP

Analysis Results

Back | Download

Analysis Name: [redacted]IonXpress_005_v1_c74... **MAPD**: 0.603

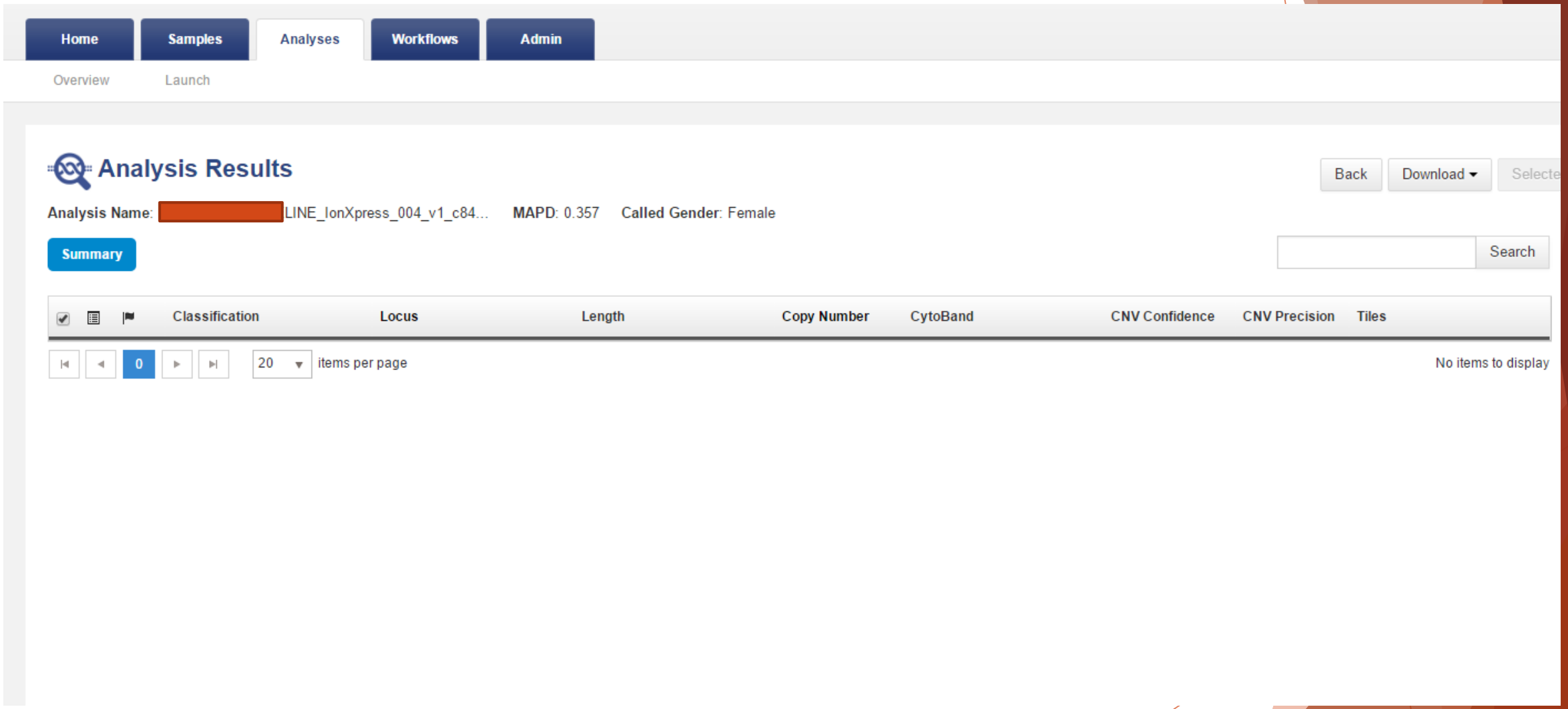
Summary

Classification	Locus	Length	Copy Number	CytoBand	CNV Confidence	CNV Precision	Tiles
Unclassified	chr1:10000	249230.621kb	2	1p36.33q44(10000-249240621)x2	0	27.1221	123
Unclassified	chr2:10000	243179.373kb	2	2p25.3q37.3(10000-243189373)x2	0	22.5848	120
Unclassified	chr3:10000	198002.43kb	2	3p26.3q29(10000-198012430)x2	0	28.3277	97
Unclassified	chr4:10000	191134.276kb	2	4p16.3q35.2(10000-191144276)x2	0	11.0814	94
Unclassified	chr5:10000	180895.26kb	2	5p15.33q35.3(10000-180905260)x2	0	6.77568	89
Unclassified	chr6:10000	171095.067kb	2	6p25.3q27(10000-171105067)x2	0	19.3982	84
Unclassified	chr7:10000	159118.663kb	2	7p22.3q36.3(10000-159128663)x2	0	15.9294	78
Unclassified	chr8:10000	146344.022kb	2	8p23.3q24.3(10000-146354022)x2	0	15.768	72
Unclassified	chr9:10000	141193.431kb	3	9p24.3q34.3(10000-141203431)x3	1.09187	1.09187	69
Unclassified	chr10:10000	135514.747kb	2	10p15.3q26.3(10000-135524747)x2	0	14.6627	67
Unclassified	chr11:10000	134986.516kb	2	11p15.5q25(10000-134996516)x2	0	6.10641	66
Unclassified	chr12:10000	34846.694kb	3	12p13.33p11.1(10000-34856694)x3	1.06049	1.06049	17
Unclassified	chr12:37856694	95985.201kb	2	12q11q24.33(37856694-133841895)x2	0	1.4203	48
Unclassified	chr13:10000	115149.878kb	2	13p13q34(10000-115159878)x2	0	14.4691	56

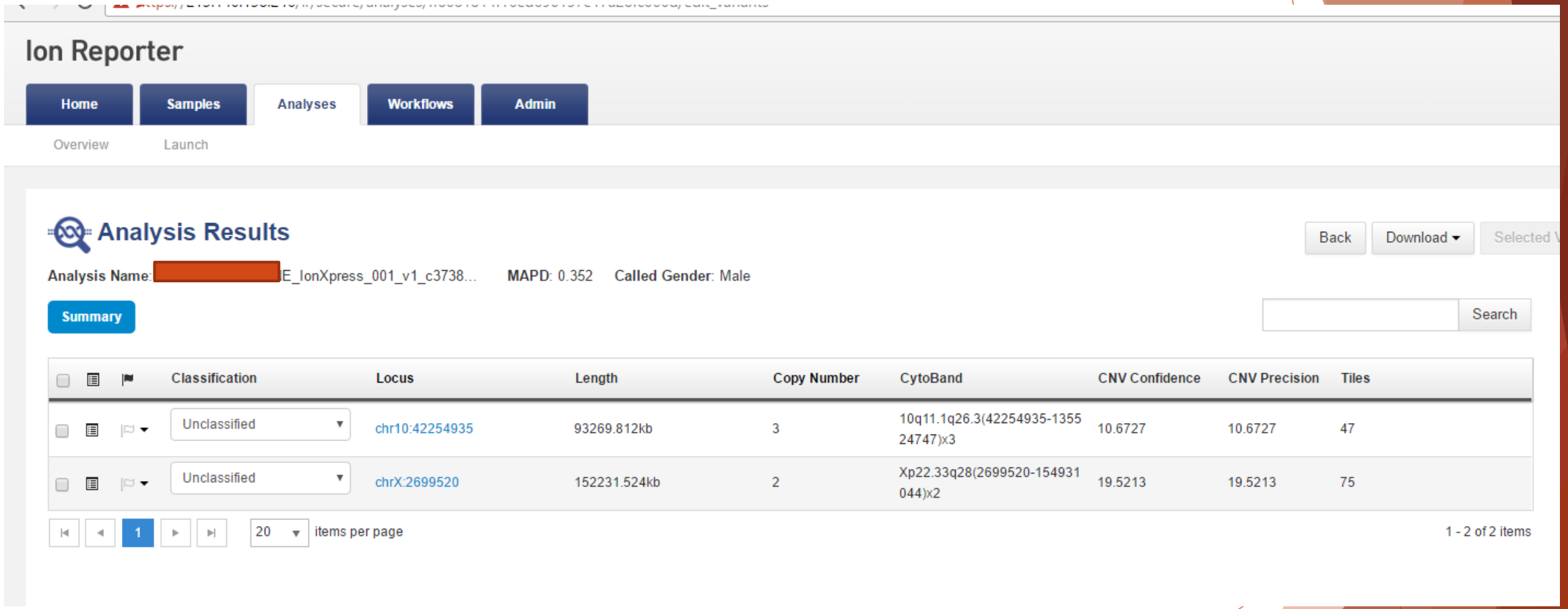
NL Male, E2 OSK

Unclassified	chr1:10000	249230.621kb	2	1p36.33q44(10000-249240621)x2	0	30.2791	123
Unclassified	chr2:10000	243179.373kb	2	2p25.3q37.3(10000-243189373)x2	0	10.1571	120
Unclassified	chr3:10000	198002.43kb	2	3p26.3q29(10000-198012430)x2	0	15.4332	97
Unclassified	chr4:10000	191134.276kb	2	4p16.3q35.2(10000-191144276)x2	0	29.8475	94
Unclassified	chr5:10000	180895.26kb	2	5p15.33q35.3(10000-180905260)x2	0	56.8275	89
Unclassified	chr6:10000	171095.067kb	2	6p25.3q27(10000-171105067)x2	0	36.1666	84
Unclassified	chr7:10000	159118.663kb	2	7p22.3q36.3(10000-159128663)x2	0	38.3783	78
Unclassified	chr8:10000	146344.022kb	2	8p23.3q24.3(10000-146354022)x2	0	29.5374	72
Unclassified	chr9:10000	141193.431kb	2	9p24.3q34.3(10000-141203431)x2	0	30.2463	69
Unclassified	chr10:10000	39244.935kb	3	10p15.3p11.1(10000-39254935)x3	3.0417	3.0417	20
Unclassified	chr10:42254935	93269.812kb	2	10q11.1q26.3(42254935-135524747)x2	0	1.59087	47
Unclassified	chr11:10000	134986.516kb	2	11p15.5q25(10000-134996516)x2	0	34.8641	66
Unclassified	chr12:10000	133831.895kb	2	12p13.33q24.33(10000-133841895)x2	0	32.5618	65
Unclassified	chr13:10000	115149.878kb	2	13p13q34(10000-115159878)x2	0	21.4565	56
Unclassified	chr14:10000	107329.54kb	2	14p13q32.33(10000-107339540)x2	0	23.1811	52
Unclassified	chr15:10000	102511.392kb	2	15p13q26.3(10000-102521392)x2	0	16.7343	49
Unclassified	chr16:10000	90334.753kb	2	16p13.3q24.3(10000-90344753)x2	0	10.9205	44
Unclassified	chr17:0	81195.21kb	2	17p13.3q25.3(0-81195210)x2	0	10.6374	39
Unclassified	chr18:10000	78057.248kb	2	18p11.32q23(10000-78067248)x2	0	8.9877	38
Unclassified	chr19:10000	59108.983kb	2	19p13.3q13.43(10000-59118983)x2	0	4.33832	28
Unclassified	chr20:10000	63005.52kb	2	20p13q13.33(10000-63015520)x2	0	7.01642	30
Unclassified	chr21:10000	48109.895kb	2	21p13q22.3(10000-48119895)x2	0	7.52378	23
Unclassified	chr22:10000	51284.566kb	3	22p13q13.33(10000-51294566)x3	1.0289	1.0289	24
Unclassified	chrX:2699520	152231.524kb	1	Xp22.33q28(2699520-154931044)x1	0	100.506	75
Unclassified	chrY:2649520	56160.48kb	1	Yp11.31q12(2649520-58810000)x1	0	12.6053	26

NL Female, E2 SEP



E1 NI Trisomy 10, XXY



PGT-A/SR using NGS

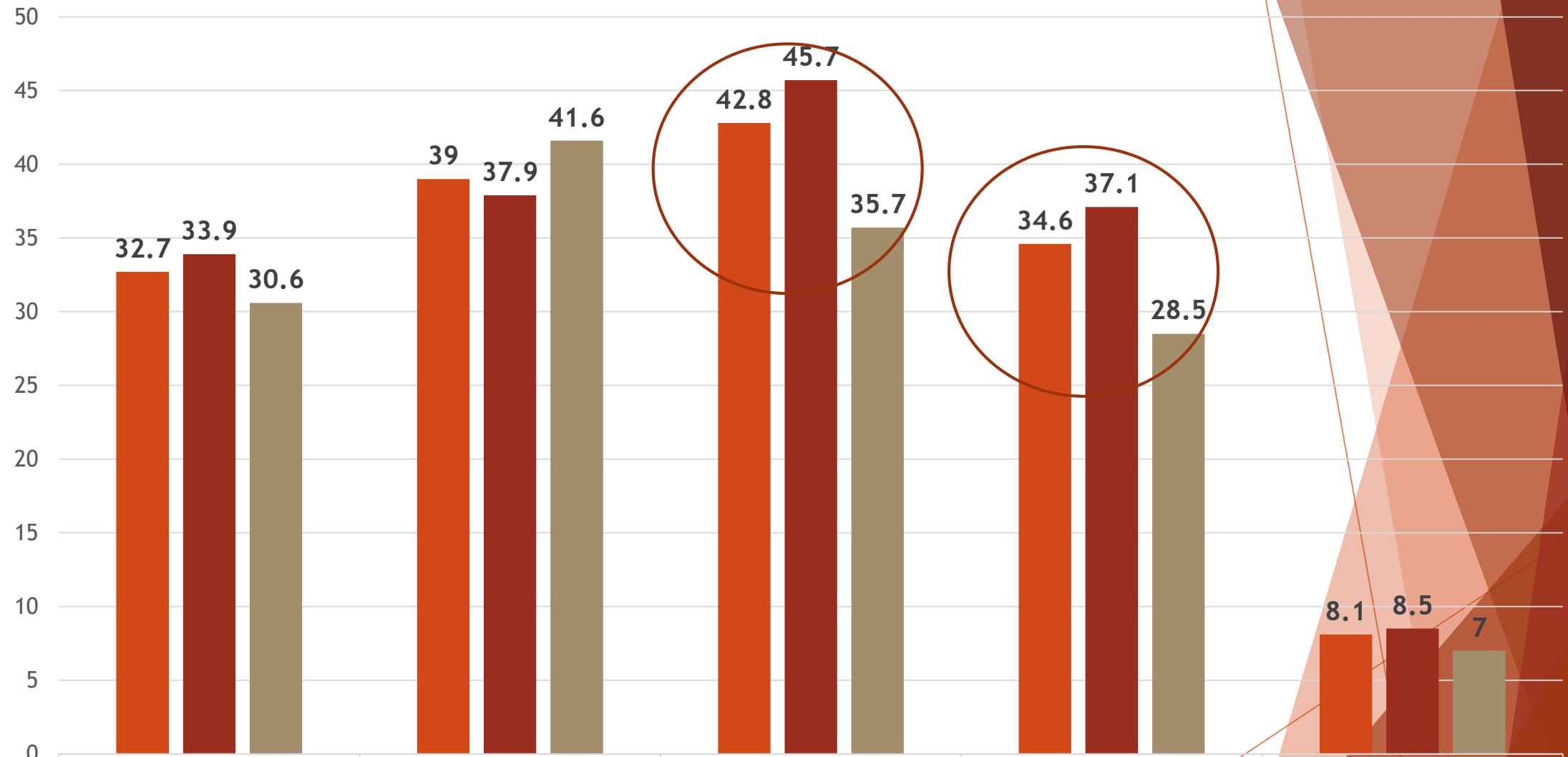
- PGT-A: 61 couples
  - Infertility or repeated implantation failure (with/without abortion): 47
  - Recurrent abortion: 14
- PGT-SR: 30
  - Chromosome abnormality in female: 12
  - Chromosome abnormality in male: 18
- PGT-A/M: 2
  - PGD-PGS-NGS (Leber congenital amaurosis): 1
  - PGD-PGS-NGS (Meckel-Gruber syndrome): 1
- Total No. of investigated embryos: **410**

PGT-A/M

- Total families: 63
- Total number of embryos: **267**
  - Euploid: **104 (39%)**
  - Aneuploid: **163 (61%)**

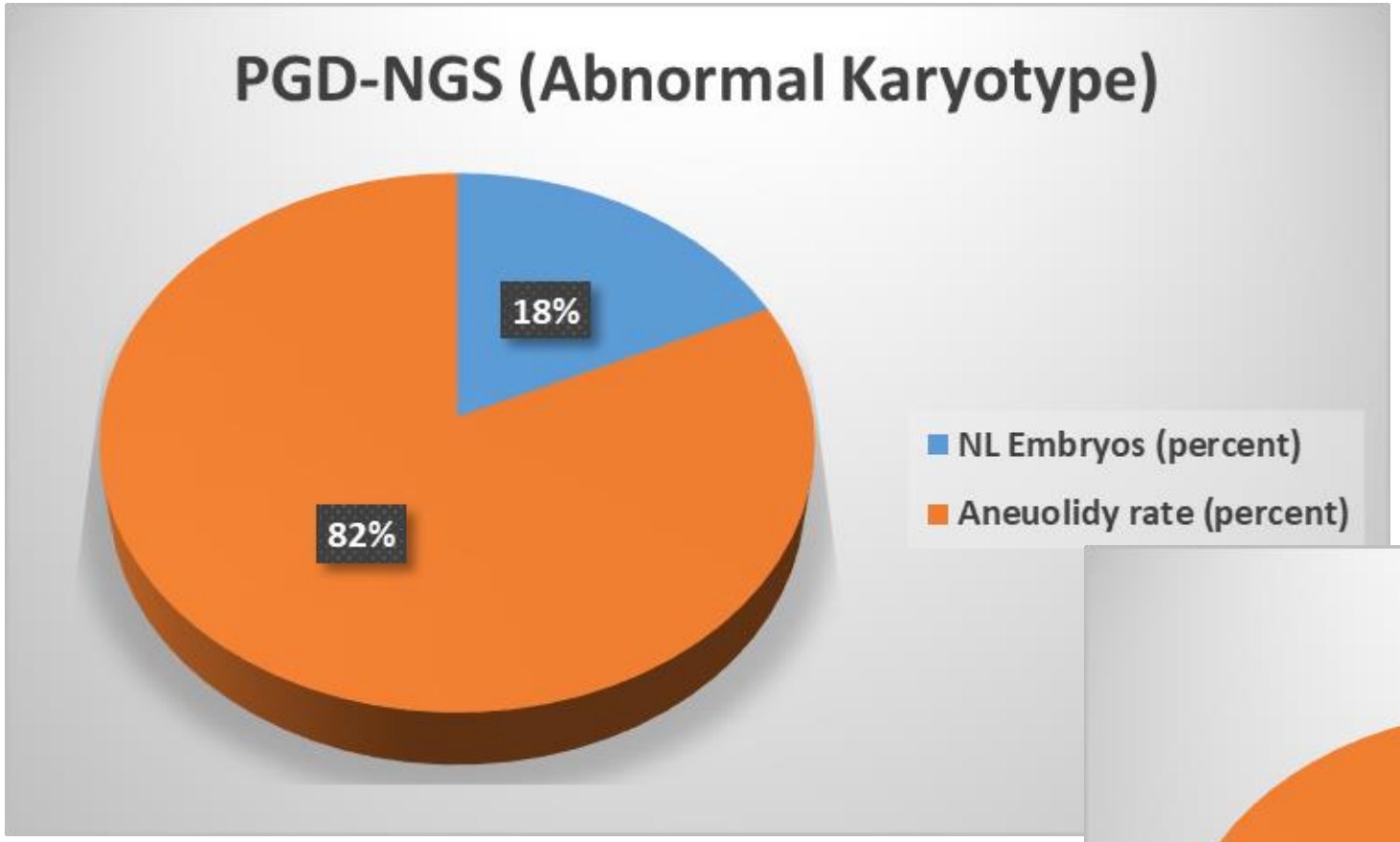
- Average maternal age: **32.7 Y**
  - **Not trransferred yet: 9 couples**

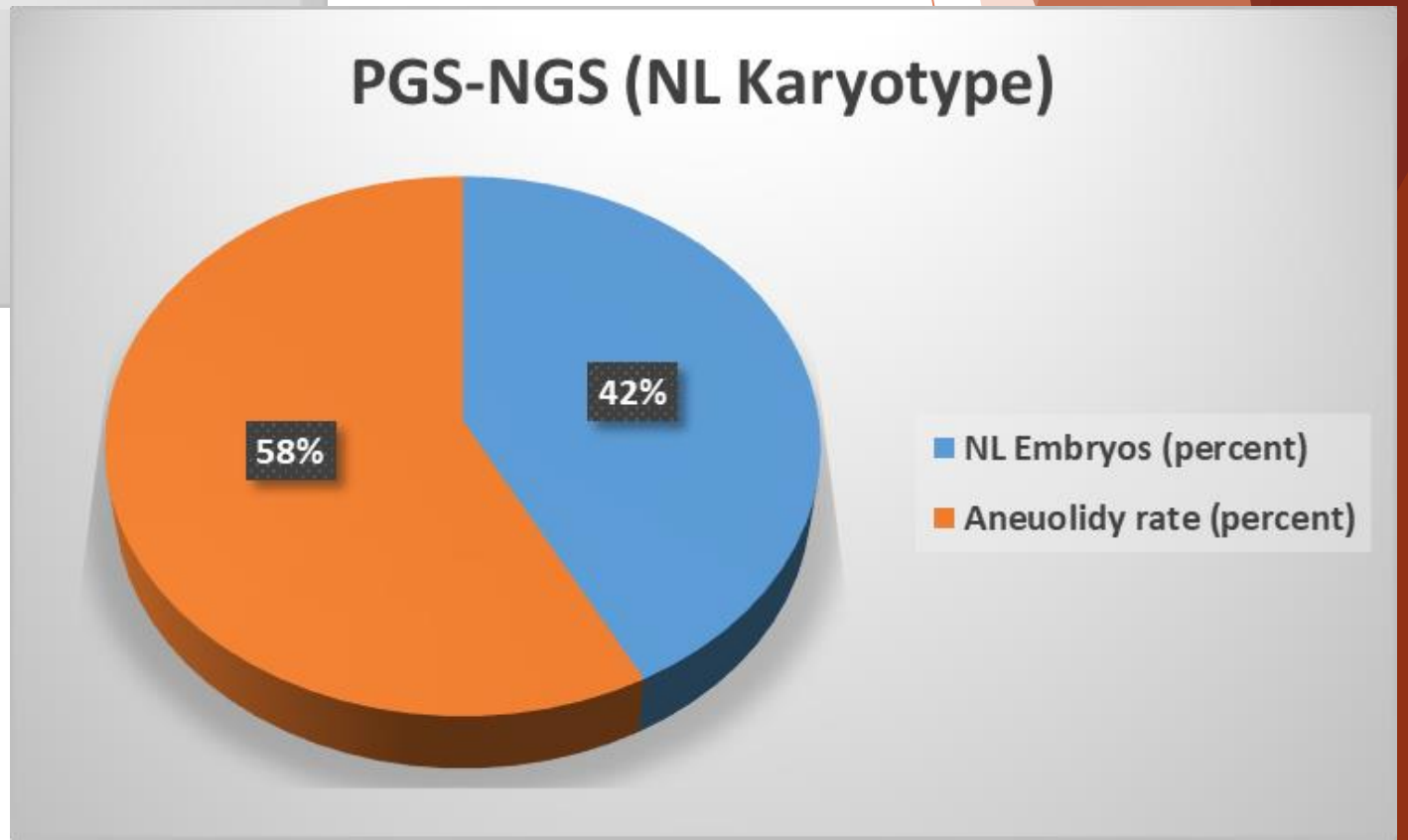
PGT-A



	Average maternal age (Y)	Euploid embryos (%)	Implantation rate (%)	live birth rate (%)	Abortion rate (%)
Total PGT-A	32.7	39	42.8	34.6	8.1
PGT-A RIF	33.9	37.9	45.7	37.1	8.5
PGT-A Rec. Ab	30.6	41.6	35.7	28.5	7

Total PGT-A PGT-A RIF PGT-A Rec. Ab


PGD-NGS (Abnormal Karyotype)
18%
82%
NL Embryos (percent)
Aneuolidy rate (percent)


PGS-NGS (NL Karyotype)
42%
58%
NL Embryos (percent)
Aneuolidy rate (percent)

PGT-SR

- Total No. of couples: **30**
- Total No. of embryos: **143**
  - Euploid and no unbalanced chr. abnormality: **23 (16%)**
  - Unbalanced chr. Abnormality: **108 (75%)**

- Average maternal age: **32.1 Y**
- Not transferred yet: **2**

PGT-SR

- ICSI cycles: 31
- Transfer cycles: **19**
  - 1 transfer cycle per family: 12
  - 2 transfer cycle per family: 2
  - 3 transfer cycles per family: 1

- Per ICSI cycle:
  - **Implantation rate : 3/14 (21.4%)**
  - **Clinical pregnancy/live birth rate: 3/14 (21.4%)**
  - Abortion rate: 0/14 (0%)

- Per transfer cycle:
  - **Implantation rate : 3/19 (15.8%)**
  - **Clinical pregnancy/live birth rate: 3/19 (15.8%)**
  - Abortion rate: 0/19 (0%)

Thank you all!